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May 29, 2019

No.: 19-71324
Short Title: NRDC v. USEPA, et al

Dear Petitioner/Counsel

A petition for writ of mandamus and/or prohibition has been received in the Clerk's Office of the United States Court of Appeals for the Ninth Circuit. The U.S. Court of Appeals docket number shown above has been assigned to this case. Always indicate this docket number when corresponding with this office about your case.

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Pursuant to Circuit Rule 21-2, an application for writ of mandamus and/or prohibition shall not bear the name of the district court judge concerned. Rather, the appropriate district court shall be named as respondent.

No. _____

IN THE
United States Court of Appeals for the Ninth Circuit

IN RE NATURAL RESOURCES DEFENSE COUNCIL, INC.,

Petitioner,

v.

U.S. ENVIRONMENTAL PROTECTION AGENCY, and ANDREW WHEELER, in his capacity as Administrator of the United States Environmental Protection Agency,

Respondents.

PETITION FOR A WRIT OF MANDAMUS

Mae Wu
Aaron Colangelo
Natural Resources Defense Council
1152 15th Street NW, Suite 300
Washington, DC 20005
(202) 289-6868
mwu@nrdc.org
acolangelo@nrdc.org

Ian Fein
Natural Resources Defense Council
111 Sutter Street, 21st Floor
San Francisco, CA 94104
(415) 875-6147
ifein@nrdc.org

Counsel for Petitioner

CORPORATE DISCLOSURE STATEMENT

Pursuant to Federal Rule of Appellate Procedure 26.1, Petitioner Natural Resources Defense Council, Inc. (NRDC) states as follows: NRDC is a non-profit corporation with no parent corporation and no outstanding stock shares or other securities in the hands of the public. NRDC does not have any parent, subsidiary, or affiliate that has issued stock shares or other securities to the public. No publicly held corporation owns any stock in NRDC.

Dated: May 29, 2019

/s/ *Ian Fein*
Ian Fein

Counsel for Petitioner

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INTRODUCTION

Ten years ago, Natural Resources Defense Council (NRDC) filed an administrative petition with the Environmental Protection Agency (EPA) to discontinue the use of a dangerous pesticide in household pet products, like flea collars and shampoos. NRDC demonstrated in its petition that these pet products threaten the neurodevelopment of young children, who are exposed to the toxic pesticide when they pet, play with, and even sleep with treated pets.

For more than two years, EPA's staff scientists have conceded these serious health risks. In a final risk assessment issued in December 2016, EPA acknowledged that epidemiology studies have consistently found neurodevelopmental effects associated with this class of pesticides, and that children's exposure from these pet products exceed the agency's level of concern. EPA recognized that "there is a need to protect children from exposures that may cause these effects."

Despite acknowledging this need, however, and despite having previously represented to this Court that it would act on NRDC's administrative petition within 90 days of issuing that final risk assessment, EPA—under the current administration—has done

nothing. Instead, the agency has opted to leave this dangerous pesticide on store shelves and in children's homes, where it continues to threaten their developing brains.

EPA's years-long delay is unreasonable and—given the acknowledged threat to children's health—unacceptable. It is also, unfortunately, of a piece with EPA's treatment of similar dangerous pesticides that have required this Court's repeated intervention. *See, e.g.*, *In re Pesticide Action Network N. Am.*, 798 F.3d 809, 811 (9th Cir. 2015) (granting mandamus and ordering EPA to "issue a full and final response" to NRDC's administrative petition to ban a related pesticide); *League of United Latin Am. Citizens v. Wheeler*, 922 F.3d 443, 443 (9th Cir. 2019) (en banc) (mem.) (granting mandamus, again, and ordering EPA to issue a "full and final decision" that resolves administrative proceedings regarding that same petition).

This Court should not allow EPA to indefinitely drag out administrative proceedings that affect the health of millions of young children. The Court should order EPA to resolve NRDC's petition forthwith—as EPA itself told this Court it would do more than two years ago.

JURISDICTION

NRDC filed its administrative petition with EPA pursuant to the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), 7 U.S.C. §§ 136 *et seq.*, and the Administrative Procedure Act (APA), 5 U.S.C. §§ 500 *et seq.* This Court would have jurisdiction to review EPA's final decision resolving NRDC's petition, *see* 7 U.S.C. § 136n(b); *United Farm Workers of Am. v. EPA*, 592 F.3d 1080, 1082-83 (9th Cir. 2010), and venue would be proper here, *see* Decl. of Gina Trujillo ¶ 3 (APP003). This Court therefore also has jurisdiction to issue a writ of mandamus compelling EPA's unreasonably delayed decision. *See* 28 U.S.C. § 1651(a); *In re A Community Voice*, 878 F.3d 779, 783 (9th Cir. 2017).

NRDC has standing to bring this action. EPA's failure to resolve NRDC's administrative petition allows manufacturers to continue selling household pet products that contain a dangerous pesticide. This injures NRDC members whose young children risk being exposed to the pesticide that threatens their health. *See* Decl. of Kelley Kruze ¶¶ 6-8, 12 (APP007-009); *NRDC v. EPA*, 735 F.3d 873, 878-79 (9th Cir. 2013). It also injures NRDC members who risk exposure to the pesticide at work. *See* Decl. of Diana Owens ¶¶ 4-15 (APP012-014); *NRDC v. FDA*, 710

F.3d 71, 81-85 (2d Cir. 2013). A favorable decision ordering EPA to resolve NRDC's petition could reduce—and potentially eliminate—these risks by prompting the agency to discontinue the pesticide's use. Protecting the public from harmful pesticides is also germane to NRDC's organizational mission, Trujillo Decl. ¶¶ 5-6 (APP003), and the requested relief does not require members' individual participation. *Hunt v. Wash. State Apple Advert. Comm'n*, 432 U.S. 333, 343 (1977).

STATUTORY FRAMEWORK

FIFRA governs the sale, use, and distribution of pesticides in the United States. *See NRDC v. EPA*, 857 F.3d 1030, 1033 (9th Cir. 2017). The statute prohibits the sale or distribution of a pesticide unless it is "registered" by EPA. 7 U.S.C. § 136a(a); *Pollinator Stewardship Council v. EPA*, 806 F.3d 520, 522 (9th Cir. 2015). EPA may not register a pesticide if it determines the pesticide would cause "unreasonable adverse effects" on human health or the environment. 7 U.S.C. §§ 136(bb), 136a(c)(5)(C); *Nw. Coal. for Alternatives to Pesticides v. EPA*, 544 F.3d 1043, 1045 (9th Cir. 2008). EPA must periodically review a pesticide's registration to evaluate whether new information warrants restricting the pesticide's use or canceling its registration. 7 U.S.C.

§ 136a(g); *Ctr. for Biological Diversity v. EPA*, 847 F.3d 1075, 1086 n.11 (9th Cir. 2017).

Any interested person can petition EPA to cancel a registered pesticide under FIFRA. *Wash. Toxics Coalition v. EPA*, 413 F.3d 1024, 1031 (9th Cir. 2005); *see also Merrell v. Thomas*, 608 F. Supp. 644, 647 (D. Or. 1985), *aff'd*, 807 F.2d 776 (9th Cir. 1986). The APA requires that the agency resolve a petition presented to it "within a reasonable time." 5 U.S.C. § 555(b); *Pesticide Action Network*, 798 F.3d at 813. If EPA determines that a registered pesticide causes unreasonable risks, it may initiate proceedings to cancel the registration. 7 U.S.C. § 136d(b).

FACTUAL BACKGROUND

NRDC petitions EPA to ban the use of a dangerous pesticide in household pet products

The pesticide at issue in this case, tetrachlorvinphos (TCVP), belongs to a class of pesticides called organophosphates, which were developed from nerve warfare agents and cause overstimulation of the nervous system. *See NRDC v. EPA*, 658 F.3d 200, 205 (2d Cir. 2011). Organophosphate exposure is particularly troubling for young children, whose neurological systems are still developing. It has been found to result in reduced cognitive capacity (i.e., lower IQ), delays in motor

development, and behavioral problems, including attention deficit/hyperactivity disorder. *See* Decl. of Miriam Rotkin-Ellman ¶¶ 7-8 (APP019-020) (discussing scientific studies).

EPA nonetheless has allowed TCVP to be used in the home—in the form of flea and tick shampoos, powders, and collars for dogs and cats—where children are exposed to it when they pet or play with treated pets. *See* EPA, Reregistration Eligibility Decision for Tetrachlorvinphos (TCVP), at 36 (July 31, 2006), *available at* https://archive.epa.gov/pesticides/reregistration/web/pdf/tcvp_red.pdf.

In 2008, a published, peer-reviewed study confirmed that TCVP was making its way into children's bodies: the study documented measurable levels of the pesticide in the urine of children who had been exposed to pets wearing TCVP flea collars. *See* M. Keith Davis et al., *Assessing Intermittent Pesticide Exposure from Flea Control Collars Containing the Organophosphorus Insecticide Tetrachlorvinphos*, 18 J. Exposure Sci. & Envtl. Epidemiology 564, 568-69 (2008). The study also documented that routine interactions with treated pets exposed people to the pesticide by transferring significant amounts of TCVP residue from the treated animal to the person's hands and clothes. *Id.* The

study estimated that there are potentially "millions of children who could be in direct contact" with TCVP via their pets. *Id.* at 564.

In April 2009, NRDC filed an administrative petition with EPA to cancel the registration of TCVP pet products. *See* NRDC, Petition to Cancel All Pet Uses for the Pesticide Tetrachlorvinphos (Apr. 23, 2009) (APP029-034). The petition highlighted the pesticide's significant health risks, as identified in recent studies. For example, the petition noted that TCVP residue levels measured in the peer-reviewed 2008 study indicated that children's routine activities with treated pets put them at risk of unsafe exposure. *Id.* at 6 (APP034).

The petition observed that EPA had "improperly permitted the continued use of [TCVP] in pet collars, which has left toddlers . . . exposed to dangerous levels of a toxic pesticide." *Id.* NRDC implored EPA to "exercise its statutory obligation to protect children by canceling all pet uses of [TCVP]." *Id.*

EPA tells this Court it will issue a final decision on NRDC's petition within 90 days of finalizing a risk assessment

Five years after filing its administrative petition, NRDC had heard nothing in response. So NRDC sought a writ of mandamus in the D.C. Circuit directing EPA to respond to the petition. *See* Am. Pet. for

Writ of Mandamus, *In re NRDC*, No. 14-1017, ECF No. 1487402 (D.C. Cir. Apr. 8, 2014) (APP036-059). Only then did EPA act, denying NRDC's petition in November 2014. *See* EPA, Response to NRDC's April 23, 2009 Petition Requesting Cancellation of All Pet Uses of TCVP (Nov. 6, 2014) (APP061-072).

NRDC promptly sued again, challenging EPA's denial in this Court as unlawful. *See* Pet. for Review, *NRDC v. EPA*, No. 15-70025, ECF No. 1-2 (9th Cir. Jan. 5, 2015) (APP074-075).[1] However, once briefing was underway, EPA announced that it wanted to reassess the risks posed by the pesticide instead of defending its denial of NRDC's petition, and so moved for a voluntary remand. *See* EPA Mot. for Voluntary Remand, ECF No. 22-1 (Sept. 25, 2015) (APP077-086).

Concerned about EPA's history of delay in these and similar proceedings, *see, e.g.*, *Pesticide Action Network*, 798 F.3d at 812-15; Rotkin-Ellman Decl. ¶¶ 21-22 (APP025), NRDC opposed the motion for an open-ended remand. NRDC instead asked this Court to ensure timely resolution of the remanded proceedings—by, for example, retaining jurisdiction or imposing a deadline on the agency. *See* NRDC

[1] All ECF citations hereinafter are to the docket in this earlier case.

Resp. to Renewed Mot. for Voluntary Remand at 16-18, ECF No. 27 (Feb. 25, 2016) (APP143-145). EPA opposed those requests and assured the Court that it was "committed to completing remand proceedings in a reasonable time frame." EPA Reply ISO Renewed Mot. at 11, ECF No. 28 (Mar. 10, 2016) (APP160).

Specifically, EPA asserted that it "intends to issue a revised response to NRDC's petition within 90 days after finalizing the [TCVP] risk assessment."[2] EPA Renewed Mot. for Voluntary Remand at 10, ECF No. 26 (Feb. 11, 2016) (APP124). The agency repeated this assertion several times. *See, e.g.*, *id.* at 5 (APP119); EPA Reply ISO Renewed Mot. at 12-13 (APP161-162); Decl. of Richard P. Keigwin, Jr. ¶ 9, ECF No. 22-2 (Sept. 25, 2015) (APP091). EPA also argued that a deadline on the remanded proceedings was unnecessary because "[m]andamus is the appropriate remedy for any unreasonable delay." EPA Renewed Mot. for Voluntary Remand at 9 n.8 (APP123); *see also* EPA Reply ISO Renewed Mot. at 15 (APP164).

[2] A risk assessment is the method by which EPA determines whether a pesticide poses unreasonable risks to human health or the environment. *Cf. NRDC*, 658 F.3d at 207-09 (discussing EPA's risk assessment methodology in the context of another organophosphate pesticide).

In June 2016, the Court remanded the case to the agency without imposing a deadline. *See* Order, ECF No. 30 (June 9, 2016) (APP168).

EPA finalizes a risk assessment that acknowledges serious health risks to young children

On December 21, 2016, EPA issued a final risk assessment for TCVP that corroborated NRDC's longstanding concerns and found health risks for young children that exceed acceptable levels. EPA, TCVP Revised Human Health Risk Assessment, at 9-10, 57-59 (Dec. 21, 2016) (APP178-179, 226-228). Among other things, the risk assessment recognized that epidemiology studies have "consistently identified" neurodevelopmental effects associated with organophosphate exposure, including "delays in mental development in infants (24-36 months), attention problems and autism spectrum disorder in early childhood, and intelligence decrements in school age children." *Id.* at 30 (APP199). EPA acknowledged that "there is a need to protect children from exposures that may cause these effects," *id.*, and that—based on the 2008 peer-reviewed study mentioned above, *see supra* at 6-7—"more stringent regulatory restrictions are necessary to protect public health," EPA, EPA's Reliance on Data from Human Research on TCVP Exposure from Pet Collars, at 1 (Dec. 21, 2016) (APP367).

One week later, EPA counsel reaffirmed to NRDC that "[i]t is EPA's current intention and belief that the Agency will issue a final revised response to NRDC's 2009 petition to cancel all pet uses of TCVP within 90 days." Email from Benjamin Wakefield, EPA Office of General Counsel, to Ian Fein (Dec. 28, 2016, 3:39 pm) (APP382).

In January 2017, EPA issued a press release announcing that the TCVP risk assessment "identified potential risks to people, including children," that "exceed the Agency's level of concern." Press Release, EPA, EPA Finalizes Human Health Risk Assessment for Pesticide Used on Pets (Jan. 4, 2017), https://www.epa.gov/pesticides/epa-finalizes-human-health-risk-assessment-pesticide-used-pets (APP379). The press release "advise[d] consumers to take certain precautions when handling TCVP products," and asserted that the agency "will issue" a proposed decision on TCVP's registration in 2017. *Id.*

EPA fails to issue a final decision on NRDC's petition

In March 2017, ninety days after EPA finalized its TCVP risk assessment, the agency did not issue a final revised response to NRDC's cancellation petition, as it had repeatedly represented that it would. Instead, EPA sent NRDC a perfunctory one-page letter, which stated, in

relevant part, that "EPA intends to address any risk-mitigation issues for the pet-care uses of TCVP when it addresses risk-mitigation issues for all TCVP products in the course of registration review for the chemical." Letter from Yu-Ting Guilaran, EPA Dir. of Pesticide Re-evaluation Div., to Mae Wu, NRDC (Mar. 21, 2017) (APP386).

At the time, EPA's publicly available registration review schedule reported that the agency intended to issue a proposed interim decision on TCVP's registration between July and September 2017. *See* EPA, Registration Review Schedules, 2017 Registration Review Schedule for Conventional Cases (as of 02/09/2017) (APP388, 393). EPA staff told the manufacturer of TCVP pet products that "EPA's timeline is spurred by its obligation to respond to NRDC's petition [to cancel] the pet uses." EPA, Notes and Action Items for 7/11/17 Teleconference with Hartz (APP395). The agency explained that "TCVP has had multiple risk assessments" as well as "multiple public comment periods," and that the agency "needed to respond to NRDC's petition." EPA, Notes and Action Items for 8/7/17 Teleconference with Hartz (APP398).

In September 2017, however, EPA did not issue a proposed decision on TCVP, as it previously said it would. Instead, EPA released

a new registration review schedule, which—unlike the prior version—omitted any reference to TCVP. *See* EPA, Registration Review Schedules, 2018 Registration Review Schedule for Conventional Cases (as of 09/18/2017) (APP400-403). Subsequent schedules have likewise included no reference to TCVP—indicating that EPA no longer plans to issue a proposed decision on its registration any time soon. *See, e.g.*, EPA, Registration Review Schedules, 2019-2020 Registration Review Schedule for Conventional Cases (as of 03/26/2019) (APP411-415).

In the meantime, TCVP continues to be sold in household pet products, where it threatens the neurodevelopment of young children who are exposed to the pesticide through residues on treated pets.

ARGUMENT

EPA's failure to resolve NRDC's petition to cancel the registration of TCVP pet products is unreasonable. NRDC filed its petition a decade ago, and more than two years have passed since EPA scientists conceded that the products threaten children's neurodevelopment. Yet EPA has taken no further public action to address the issue, despite having previously represented publicly—and to this Court—that it would act on the pesticide's registration in 2017. Meanwhile, young

children continue to be exposed to the toxic pesticide when they pet and play with treated pets.

More than once in recent years, this Court has concluded that EPA unreasonably delayed resolving administrative petitions which sought to protect the public health. *See Community Voice*, 878 F.3d at 786-87 (granting mandamus and ordering EPA to finalize a rulemaking regarding lead paint standards); *Pesticide Action Network*, 798 F.3d at 814 (granting mandamus and ordering EPA to issue a full and final response to NRDC's petition to ban the use of a dangerous pesticide); *League of United Latin American Citizens*, 922 F.3d at 443 (granting mandamus, again, and ordering EPA to resolve administrative proceedings regarding that same petition and pesticide).

Two questions are at issue in such cases: (1) whether the agency has a duty to act and, if so, (2) whether its delay in taking that action is unreasonable. *Community Voice*, 878 F.3d at 784. Here, as in the other recent cases, EPA has a duty to resolve NRDC's petition within a reasonable time, 5 U.S.C. § 555(b), and this case is similar in its length of delay, absence of a concrete timeline, and harm to children's health, *Community Voice*, 878 F.3d at 786. EPA has also repeatedly broken its

commitments to the Court, to NRDC, and to the public that it would timely resolve NRDC's petition and take action on TCVP. *See Pesticide Action Network*, 798 F.3d at 814. Thus, like in the other recent cases, the Court should order EPA to resolve NRDC's petition forthwith.

I. EPA has a legal duty to resolve NRDC's petition and decide whether to ban TCVP pet products

"EPA has a clear duty to act under the APA." *Community Voice*, 878 F.3d at 784. The APA requires that agencies "shall" "conclude a matter presented to it" "within a reasonable time." 5 U.S.C. § 555(b). This "general but nondiscretionary duty," *Mashpee Wampanoag Tribal Council, Inc. v. Norton*, 336 F.3d 1094, 1099 (D.C. Cir. 2003), extends to administrative petitions that are "requests for discretionary action," *In re Am. Rivers & Idaho Rivers United*, 372 F.3d 413, 418 (D.C. Cir. 2004). That is, an agency is "obligated *under the APA*" to resolve petitions presented to it, even if the agency may have some discretion regarding the final action it ultimately takes. *Id.* at 419. "An agency 'cannot simply refuse to exercise [its] discretion' to conclude a matter." *Community Voice*, 878 F.3d at 785 (alteration in original) (quoting *Indep. Min. Co. v. Babbitt*, 105 F.3d 502, 507 n.6 (9th Cir. 1997)). Thus,

NRDC is entitled to a "final ruling" on its petition—i.e., a "formal action to grant or deny it." *Pesticide Action Network*, 798 F.3d at 813.[3]

Nor does EPA's short, noncommittal letter in March 2017 satisfy its duty to "*conclude* [the] matter presented to it." 5 U.S.C. § 555(b) (emphasis added); *see* Letter from Yu-Ting Guilaran (APP386). "To 'conclude [the] matter,' EPA must enter a final decision subject to judicial review." *Community Voice*, 878 F.3d at 785 (alteration in original); *see also Pub. Citizen Health Research Grp. v. Comm'r, FDA*, 740 F.2d 21, 32 (D.C. Cir. 1984) (the APA requires that agencies "*resolve* the questions in issue within a reasonable time" (emphasis added)). Yet EPA's March 2017 letter provides neither a "*full* [nor] *final* response to the administrative petition." *Pesticide Action Network*, 798 F.3d at 815 (emphases added). Instead, the letter merely kicks the can down the road, with no concrete timetable or commitment for further

[3] Indeed, EPA effectively conceded that it has a duty to resolve NRDC's administrative petition when it acknowledged to this Court that mandamus would be an "appropriate remedy" for any unreasonable delay following the earlier remand. EPA Renewed Mot. for Voluntary Remand at 9 n.8 (APP123); *see also* EPA Reply ISO Renewed Mot. at 15 (APP164) ("mandamus, not a schedule on remand, is the appropriate relief if there were such a delay").

action. Indeed, EPA acknowledged—after the March 2017 letter—that it still had an "obligation to respond to NRDC's petition." EPA Notes and Action Items 7/11/17 (APP395); *see also* EPA Notes from Teleconference 8/7/17 (APP398) (acknowledging that EPA "needed to respond to NRDC's petition"). Thus, as EPA itself has conceded, the agency still must "fully respond" to NRDC's administrative petition and "reach some final decision." *Community Voice*, 878 F.3d at 785-86.

Above and beyond EPA's "clear duty to act under the APA," this Court also found in *Community Voice* that EPA had a separate, "ongoing duty" to revisit its prior determinations under a "statutory framework" where Congress had directed the agency to protect children from lead poisoning and authorized it to amend its lead paint standards based on new information. 878 F.3d at 784. Here, like in that case, Congress has authorized EPA to cancel the registration of a pesticide that causes unreasonable risk to human health. 7 U.S.C. § 136d(b).

Moreover, like in *Community Voice*, "EPA does not dispute that now available information shows" that further action is warranted to protect children. 878 F.3d at 784. To the contrary, EPA now concedes that TCVP pet products pose health risks that exceed the agency's level

of concern, "creating an 'obvious need, apparent to [the EPA],'" to protect children's health. *Id.* at 785 (alteration in original) (quoting *Pub. Citizen Health Research Grp. v. Auchter*, 702 F.2d 1150, 1154 (D.C. Cir. 1983)); *see* Risk Assessment at 30 (APP199) (acknowledging "there is a need to protect children" from exposure to TCVP); EPA's Reliance on Data from Human Research on TCVP at 1 (APP367) (acknowledging, based on TCVP study, that "more stringent regulatory restrictions are necessary to protect public health"). "Under these circumstances, EPA is under a clear duty to act." *Community Voice*, 878 F.3d at 785.

In short, EPA has a "clear duty" to take final action on NRDC's 2009 petition. *Id.* at 784. A writ of mandamus is therefore appropriate if EPA's delay in taking such action has been unreasonable. *Id.* at 786. As explained below, EPA's failure to resolve NRDC's decade-old petition—despite its prior representations to this Court, and the acknowledged health risks to children—is demonstrably unreasonable.

II. EPA's delay in resolving NRDC's petition is unreasonable

This Court considers six factors—first articulated in *Telecommunications Research & Action Center v. FCC*, 750 F.2d 70 (D.C. Cir. 1984) ("*TRAC*"), and commonly referred to as the "*TRAC*

factors"—in determining whether an agency's delay is unreasonable. They are (1) whether the time the agency takes to make a decision complies with a "rule of reason"; (2) whether Congress has provided a timetable for the agency's action; (3) whether human health is at stake; (4) the effect of expediting agency action on competing priorities; (5) the nature and extent of the interests prejudiced by the delay; and (6) any impropriety by the agency. *Community Voice*, 878 F.3d at 786.

In both *Community Voice*, 878 F.3d at 786-87, and *Pesticide Action Network*, 798 F.3d at 814, this Court concluded that it was unreasonable for EPA to take more than eight years to resolve administrative petitions that sought to protect public health, where the agency itself acknowledged the health dangers and yet still did not provide a "concrete timetable" for final action. "This case is similar in the length of delay, absence of a reasonable timetable, and harm to health." *Community Voice*, 878 F.3d at 786.

A. EPA's lengthy delay, and the absence of any timetable to resolve the petition, violates the rule of reason

The first, and "most important," *TRAC* factor weighs sharply in favor of mandamus here, as EPA's lengthy delay and the absence of any

concrete timeline to resolve NRDC's administrative petition defies any "rule of reason." *Community Voice*, 878 F.3d at 786.

NRDC filed its administrative petition to ban TCVP pet products in April 2009, more than ten years ago. *See* NRDC, Petition to Cancel All Pet Uses (APP029-034). EPA's decade-long delay in resolving that petition exceeds the eight years that were found to be unreasonable in *Community Voice*, 878 F.3d at 786-87, and *Pesticide Action Network*, 798 F.3d at 814. To be sure, EPA did take a fleeting final action when it previously denied NRDC's petition in November 2014, but the agency quickly negated that action by moving for a voluntary remand to reconsider the denial rather than defend it on the merits. *See supra* at 8. Allowing that ephemeral, earlier action to evade mandamus here would invite agencies to use voluntary remands to insulate themselves from judicial review. And it would defeat the "primary purpose of the writ in circumstances like these," which is "to ensure that an agency does not thwart [the court's] jurisdiction by withholding a reviewable decision." *American Rivers*, 372 F.3d at 419.

In any event, the "pace of [EPA's] decisional process" here defies the rule of reason no matter how one measures it. *Comm'r*, 740 F.2d at

34. "[A] reasonable time for agency action is typically counted in weeks or months, not years." *American Rivers*, 372 F.3d at 419. This Court—sitting en banc—recently found EPA's nearly two-year delay in resolving objections to its initial decision denying NRDC's petition regarding another organophosphate pesticide to be unreasonable. *League of United Latin American Citizens*, 922 F.3d at 443. The same is true here, given the "history and chronology of this matter." *Id.*

It has now been more than three and half years since EPA asked this Court to remand its prior decision denying NRDC's TCVP administrative petition, *see* EPA Mot. for Voluntary Remand (APP077-086), and nearly two and a half years since EPA finalized its risk assessment acknowledging risks of concern to young children, *see* Risk Assessment 9-10 (APP178-179). Yet EPA has taken no further action to resolve those risks or provide a full and final response to NRDC's petition. And EPA's own publicly available schedule now reveals that it no longer plans to issue even a *proposed* decision on TCVP's registration any time soon, despite having previously announced to the public that it would do so in 2017. *See supra* at 11-13. Indeed, EPA has inexplicably removed TCVP from its registration review schedule altogether. *Id.*

EPA's continued, lengthy inaction violates its representations to this Court that it was "committed to completing remand proceedings in a reasonable time frame." EPA Reply ISO Renewed Mot. at 11 (APP160). EPA urged this Court not to impose a schedule on the remand by asserting—repeatedly—that it intended to issue a revised response to NRDC's petition within 90 days of finalizing the TCVP risk assessment. *See supra* at 9. But, on remand, EPA "failed to issue a final response to the administrative petition," as it had repeatedly told this Court that it would. *Pesticide Action Network*, 798 F.3d at 812. And instead of offering a "'concrete timeline' for resolving the petition," EPA has provided only "a roadmap for further delay." *Id.* at 814.

Here, as with its decade-long deliberation regarding a related organophosphate pesticide, "EPA has stretched the 'rule of reason' beyond its limits." *Id.* at 814. "Issuing a writ of mandamus is necessary to end this cycle of incomplete responses, missed deadlines, and unreasonable delay." *Id.* at 813; *see also League of United Latin American Citizens*, 922 F.3d at 443.

B. EPA acknowledges that its delay threatens children's health

EPA's lengthy delay in resolving NRDC's administrative petition is particularly unreasonable because the agency has confirmed that TCVP pet products endanger children's neurodevelopment. "When the public health may be at stake, the agency must move expeditiously to consider and resolve the issues before it." *Comm'r*, 740 F.2d at 34. The third *TRAC* factor thus favors issuance of the writ because "EPA itself has acknowledged" that its inaction poses "a clear threat to human welfare." *Community Voice*, 878 F.3d at 787.

TCVP belongs to the same class of organophosphate pesticides as chlorpyrifos, the chemical at issue in *Pesticide Action Network* and *League of United Latin American Citizens*. The agency's 2016 risk assessment for TCVP acknowledged that epidemiology studies have "consistently identified" neurodevelopmental effects associated with children's exposure to this class of pesticides, including delays in mental development, attention deficit disorders, and lower IQs. *See supra* at 5-6. And just as EPA scientists in *Pesticide Action Network* had "backtracked significantly" from any prior suggestions that chlorpyrifos was safe, 798 F.3d at 814, here too EPA's risk assessment for TCVP

found potential health effects from pet products that exceed the agency's level of concern. *See supra* at 10. EPA expressly acknowledged that "there is a need to protect children from exposures that may cause these effects." *Id.* (quoting Risk Assessment at 30 (APP199)).

EPA has offered "no acceptable justification" for refusing to resolve that compelling need. *Pesticide Action Network*, 798 F.3d at 814. In fact, "despite the documented risks" to children's neurodevelopment, EPA has provided "no reasoned explanation" at all "why it has protracted" resolution of NRDC's petition to ban TCVP pet products. *Auchter*, 702 F.2d at 1158. "In view of EPA's own assessment of the dangers to human health posed by this pesticide," the agency "should be compelled to act quickly to resolve the administrative petition." *Pesticide Action Network*, 798 F.3d at 814.

C. No competing interests or priorities justify EPA's unreasonable delay

As in *Pesticide Action Network*, the first and third *TRAC* factors are strong enough on their own here to establish the unreasonableness of EPA's lengthy delay in resolving NRDC's administrative petition. 798 F.3d at 814. Also like in that case, the remaining factors are either neutral or support the same conclusion.

To begin with, it does not matter under the second *TRAC* factor that FIFRA requires EPA to complete its registration review of all previously-registered pesticides by 2022. 7 U.S.C. § 136a(g)(1)(A)(iii)(I). Irrespective of that schedule, EPA "is obligated *under the APA* to respond to [NRDC's 2009] petition" within a reasonable time. *American Rivers*, 372 F.3d at 419; *see* 5 U.S.C. § 555(b). That is why this Court ordered EPA to issue a full and final response to NRDC's similar administrative petition in *Pesticide Action Network*, notwithstanding any separate FIFRA schedule. 798 F.3d at 814-15. And that is why EPA told a TCVP pet product manufacturer that its plan to issue a proposed decision in September 2017 was "spurred by its obligation to respond to NRDC's petition." EPA Notes and Action Items 7/11/17 (APP395).

Moreover, the registration review provision states expressly that "[n]othing in this subsection shall prohibit the Administrator from undertaking any other review of a pesticide," 7 U.S.C. § 136a(g)(1)(C), which precludes EPA from invoking that process to forestall other scientifically compelled regulatory action. *See, e.g.*, *id.* §136d(b) (providing for cancellation of registrations of pesticides that pose unreasonable adverse effects). That is especially so here, where EPA

told this Court three and a half years ago that TCVP was "*currently* undergoing registration review," Keigwin Decl. ¶ 4 (APP089) (emphasis added), and where EPA has—without explanation—since *removed* TCVP from its registration review schedule altogether, *see supra* at 13.

Nor does the fourth *TRAC* factor cut against mandamus here, where EPA has "in no way indicated that any practical impediments have prevented a response or that any agency activities of a higher or competing priority have required its attention." *American Rivers*, 372 F.3d at 420 (quotation omitted). This Court in *Pesticide Action Network* expressly "recognize[d] the scientific complexity inherent in evaluating the safety of pesticides and the competing interests that the agency must juggle." 798 F.3d at 811. The Court nonetheless concluded that mandamus was warranted where EPA had already "spent nearly a decade reviewing [NRDC's] data and arguments." *Id.* at 813. So too here. When the agency's review has spanned many years and progressed to the extent it has in this case, "scientific uncertainties and technical complexities . . . can no longer justify delay." *Pub. Citizen Health Research Grp. v. Chao*, 314 F.3d 143, 156 (3d Cir. 2002).

The fifth *TRAC* factor strongly "favors issuance of the writ" because "children exposed to [TCVP] due to the failure of EPA to act are severely prejudiced by EPA's delay." *Community Voice*, 878 F.3d at 787. There are potentially millions of children who could be in direct contact with TCVP via treated pets. *See supra* at 7. "Yet EPA offers no acceptable justification for the considerable human health interests prejudiced by [its] delay." *Pesticide Action Network*, 798 F.3d at 814.

NRDC, too, has been prejudiced by EPA's failure to resolve its administrative petition. EPA previously told this Court that NRDC would not be prejudiced by the earlier remand because the agency "will issue a new response to NRDC's petition for cancellation" after finalizing the TCVP risk assessment. EPA Reply ISO Renewed Mot. at 8 (APP157). However, because of EPA's subsequent "inaction," NRDC is now "stuck in administrative limbo; it enjoys neither a favorable ruling on its petition nor the opportunity to challenge an unfavorable one." *In re People's Mojahedin Org. of Iran*, 680 F.3d 832, 837 (D.C. Cir. 2012). The Court should not permit EPA to evade judicial scrutiny of its decisions by withholding final action following its voluntary remand.

Finally, under the sixth *TRAC* factor, this Court "need not find any impropriety lurking behind agency lassitude in order to hold that agency action is 'unreasonably delayed.'" *Comm'r*, 740 F.2d at 34. But as in *Pesticide Action Network*, EPA now has a "significant history of missing the deadlines" it has set for resolving NRDC's petition and reaching a final determination on TCVP's registration. 798 F.3d at 814.

Thus, with or without any "allegation of impropriety underlying EPA's delay," the agency's failure to adhere to its previous timelines helps demonstrate the need for relief from this Court. *Id.* Indeed, EPA's recalcitrance to resolve the issue has now "been the subject of three non-frivolous lawsuits," *id.* at 814-15, including an earlier mandamus petition, *supra* at 7-8. The Court should put "an end to [EPA's] marathon round of administrative keep-away," *American Rivers*, 372 F.3d at 420, and grant mandamus to "let [the] agency know, in no uncertain terms, that enough is enough," *Pub. Citizen Health Research Grp. v. Brock*, 823 F.2d 626, 627 (D.C. Cir. 1987).

III. The Court should grant a writ of mandamus and retain jurisdiction to ensure that EPA timely resolves the petition

NRDC respectfully requests that the Court grant a writ of mandamus and, like in *Pesticide Action Network*, "order EPA to issue a

full and final response to [NRDC's administrative] petition" by either denying the petition or issuing a proposed decision to cancel all pet uses of TCVP forthwith. 798 F.3d at 811.

This Court's authority to "compel agency action . . . unreasonably delayed," 5 U.S.C. § 706(1), gives it "discretion in determining how soon the agency must act," *Mashpee Wampanoag Tribal Council*, 336 F.3d at 1102. Although the Court gave EPA a little under 90 days to publish a proposed rule in *Pesticide Action Network*, a shorter deadline is warranted here. EPA previously represented to this Court that it needed only 90 days to issue a final response to NRDC's petition after finalizing its TCVP risk assessment—an event that occurred almost two and a half years ago. Given how much time has already passed, a shorter deadline of 60 (or fewer) days is therefore more appropriate at this juncture. *See, e.g.*, *American Rivers*, 372 F.3d at 420 (ordering agency to "issue a judicially reviewable response to [an administrative] petition within 45 days"); *Auchter*, 702 F.2d at 1159 (ordering agency to "issue a notice of proposed rulemaking within 30 days").

Moreover, if EPA issues a proposed decision to cancel TCVP's registration, NRDC respectfully requests that the Court order the

agency to finalize that decision within a year. *See Community Voice*, 878 F.3d at 788; *In re Pesticide Action Network N. Am.*, 808 F.3d 402, 402-03 (9th Cir. 2015) (ordering EPA to "take final action" on its proposed decision within roughly a year).

Finally, to ensure compliance with these deadlines, and given the lengthy history of delay in these (and similar) proceedings, NRDC respectfully requests that the Court "retain[] jurisdiction" in this case, at least "until EPA issues a final order subject to judicial review." *Community Voice*, 878 F.3d at 788; *see also, e.g.*, *League of United Latin American Citizens*, 922 F.3d at 443 (granting mandamus and "retain[ing] jurisdiction over this and any related cases").

CONCLUSION

For the foregoing reasons, the Court should grant the petition for a writ of mandamus and order EPA to issue a full and final response to NRDC's administrative petition within 60 (or fewer) days, by either denying the petition or issuing a proposed decision to cancel all pet uses of TCVP. If EPA issues a proposed decision to cancel the registration, a final decision should follow within one year. The Court should also retain jurisdiction to ensure EPA's compliance with these deadlines.

Dated: May 29, 2019

Respectfully submitted,

/s/ *Ian Fein*

Ian Fein
Natural Resources Defense Council
111 Sutter Street, 21st Floor
San Francisco, CA 94104
(415) 875-6147
ifein@nrdc.org

Mae Wu
Aaron Colangelo
Natural Resources Defense Council
1152 15th Street NW, Suite 300
Washington, DC 20005
(202) 289-6868
mwu@nrdc.org
acolangelo@nrdc.org

Counsel for Petitioner Natural Resources Defense Council

STATEMENT OF RELATED CASES

This case is related, within the meaning of Ninth Circuit Rule 28-2.6(c), to another case pending in this Court, *League of United Latin Am. Citizens v. Wheeler*, No. 17-71636 (9th Cir.), because they raise "closely related issues" about EPA's decade-long failure to resolve administrative proceedings regarding petitions to ban the use of organophosphate pesticides.

Dated: May 29, 2019

/s/ *Ian Fein*
Ian Fein

CERTIFICATE OF COMPLIANCE

This petition for a writ of mandamus complies with the type-volume limitation of Ninth Circuit Rule 21-2(c) because it does not exceed 30 pages, excluding the parts exempted by Federal Rules of Appellate Procedure 21(a)(2)(C) and 32(f).

The petition also complies with the typeface requirements of Federal Rule of Appellate Procedure 32(a)(5) and the type style requirements of Federal Rule of Appellate Procedure 32(a)(6) because it has been prepared in a proportionally spaced typeface using Microsoft Word 14-point Century Schoolbook font.

Dated: May 29, 2019

/s/ *Ian Fein*
Ian Fein

CERTIFICATE OF SERVICE

I hereby certify that I have this date served a copy of the foregoing Petition for a Writ of Mandamus upon all parties by U.S. mail at the following addresses:

Matthew Z. Leopold, General Counsel
Environmental Protection Agency
1200 Pennsylvania Avenue NW
Mail Code: 2310A
Washington, DC 20460

Andrew Wheeler, Administrator
Environmental Protection Agency
1200 Pennsylvania Avenue NW
Mail Code: 1101A
Washington, DC 20460

William P. Barr, Attorney General
U.S. Department of Justice
950 Pennsylvania Avenue NW
Washington, DC 20530

Civil Process Clerk
U.S. Attorney's Office for the Northern District of California
450 Golden Gate Avenue, 11th Floor
San Francisco, CA 94102

Dated: May 29, 2019

/s/ *Jessie Baird*
Jessie Baird

No. _____

IN THE
United States Court of Appeals
for the Ninth Circuit

IN RE NATURAL RESOURCES DEFENSE COUNCIL, INC.,

Petitioner,

v.

U.S. ENVIRONMENTAL PROTECTION AGENCY, and ANDREW WHEELER, in his capacity as Administrator of the United States Environmental Protection Agency,

Respondents.

APPENDIX

Mae Wu
Aaron Colangelo
Natural Resources Defense Council
1152 15th Street NW, Suite 300
Washington, DC 20005
(202) 289-6868
mwu@nrdc.org
acolangelo@nrdc.org

Ian Fein
Natural Resources Defense Council
111 Sutter Street, 21st Floor
San Francisco, CA 94104
(415) 875-6147
ifein@nrdc.org

Counsel for Petitioner

APPENDIX TABLE OF CONTENTS

In re NRDC v. EPA

Exhibit A

IN THE UNITED STATES COURT OF APPEALS
FOR THE NINTH CIRCUIT

IN RE NATURAL RESOURCES DEFENSE COUNCIL, INC., *Petitioner*, v. U.S. ENVIRONMENTAL PROTECTION AGENCY, et al., *Respondents*.	Case No. 19-_____

DECLARATION OF GINA TRUJILLO

I, Gina Trujillo, state as follows:

1. I am the National Director of Membership at the Natural Resources Defense Council, Inc. ("NRDC"). I have worked in the membership department of NRDC for more than 25 years.

2. My duties include supervising the maintenance of membership records and preparation of materials that NRDC distributes to members and prospective members. Those materials describe NRDC and identify its mission. I am familiar with NRDC's mission statement and its priorities.

3. NRDC is a membership organization incorporated under the laws of the State of New York. It is recognized as a not-for-profit corporation under section 501(c)(3) of the United States Internal Revenue Code. NRDC maintains offices throughout the United States, including two in California—in San Francisco and Santa Monica.

4. NRDC currently has hundreds of thousands of members nationwide. Records show that there are NRDC members living in each of the fifty states and in the District of Columbia.

5. NRDC's mission statement declares that "The Natural Resources Defense Council's purpose is to safeguard the Earth: its people, its plants and animals, and the natural systems on which all life depends."

6. Protecting the public from the substantial adverse health effects caused by exposure to toxic chemicals, such as tetrachlorvinphos ("TCVP"), is central to NRDC's purpose.

7. When a person becomes a member of NRDC, that person authorizes NRDC to take legal action on his or her behalf to protect the environment and public health.

I declare under penalty of perjury that the foregoing is true and correct, to the best of my knowledge, information, and belief. Executed on March 12, 2019, in New York, New York.

Gina Trujillo

Gina Trujillo

Exhibit B

IN THE UNITED STATES COURT OF APPEALS
FOR THE NINTH CIRCUIT

IN RE NATURAL RESOURCES DEFENSE COUNCIL, INC., *Petitioner*, v. U.S. ENVIRONMENTAL PROTECTION AGENCY, et al., *Respondents*.	Case No. 19-_____

DECLARATION OF KELLEY KRUZE

I, Kelley Kruze, declare as follows:

1. I am a member of the Natural Resources Defense Council.

2. I live in San Francisco, California, with my husband and 14-month-old son. I have bachelor's degrees in microbiology and nursing, and currently work as a registered nurse at Kaiser Permanente.

3. I am concerned about my son's exposure to harmful chemicals and pesticides, and I do what I can to avoid them. I try to feed my family only organic food. I also try to purchase only safe and earth-friendly bath and cleaning products. We even use organic sheets and mattresses. But I can't control everything my son eats or touches.

4. We also have a pet dog—a large labradoodle named Fibonacci (or Fib), who will be two years old in June. Based on the advice of our veterinarian, we give Fib an oral medicine to control ticks and fleas. Our veterinarian said that the oral treatment is more effective than topical alternatives and poses a lower risk to young kids.

5. Our son loves Fib, who is very patient with him. They've pretty much grown up together. Our son is always playing with Fib's toys or crawling around and laying with him. They spend a lot of time together when we're at home.

6. Our son likes other dogs too. We watched our neighbors' dog when they were on vacation, and our son would pet her and pull on her ears. We also take our son and Fib to dog parks quite frequently. We try to keep other dogs away from our son as much as possible, but I know that will be harder to do once our son becomes more mobile.

7. Our son often plays with one other child, typically in the other child's home. The other child's family has two pet dogs. When the weather is nice, we often take our son outside to the park or a playground. I expect that our son encounters other dogs on these outings, as there are many dogs in our neighborhood.

8. Our son is at an age where he often puts his hands in his mouth—especially when he is eating snacks, which often occurs when he is on an outing.

9. I recently learned that NRDC has been trying for several years to get EPA to ban the use of the pesticide tetrachlorvinphos (TCVP) in pet products like flea collars and shampoos. I understand that TCVP can be harmful to children and adults when they come into contact with it.

10. I grew up with a dog, and I remember our family using flea collars and other pet products like shampoos. I distinctly remember one time when I felt nauseous and sick after giving our dog a bath and soaping him with a shampoo, though I don't recall the specific brand.

11. Now, as a parent, I am worried about harm to my son from exposure to pesticides like TCVP. I feel very strongly that household products containing dangerous chemicals like TCVP should be banned. The way I look at it—if I'm not going to put these products on myself, why would I ever put them on my pet or expose my child, family, and friends to any of these harmful chemicals and pesticides?

12. As mentioned above, I do what I can to avoid my son's exposure to harmful chemicals and pesticides, including TCVP. But his

exposure is not entirely within my control. And there is no way for me to eliminate his risk of exposure to TCVP unless EPA bans it.

13. I hope that EPA will grant NRDC's petition to ban TCVP pet products, so that my son will no longer risk being exposed to the dangerous pesticide when he pets or plays with other dogs.

I declare under penalty of perjury that the foregoing is true and correct, to the best of my knowledge, information, and belief. Executed on April 22, 2019, in San Francisco, California.

Kelley Kruze

Exhibit C

IN THE UNITED STATES COURT OF APPEALS
FOR THE NINTH CIRCUIT

IN RE NATURAL RESOURCES DEFENSE COUNCIL, INC., *Petitioner*, v. U.S. ENVIRONMENTAL PROTECTION AGENCY, et al., *Respondents.*	Case No. 19-_____

DECLARATION OF DIANA OWENS

I, Diana Owens, declare as follows:

1. I am a member of the Natural Resources Defense Council. I joined in 1994 because I am concerned about public health and safety, and I appreciate how NRDC advocates for sound science-based environmental policy.

2. I live in Sarasota County, Florida, with my husband.

3. I am a certified veterinary technician in the State of Florida. To obtain certification, a technician must have a two-year college degree

and pass state and national exams. I became a technician because I love animals and am interested in science and health.

4. I have worked as a technician in a veterinary clinic since 1991. We provide all manner of nursing care and preventative health care for our client's pets.

5. The clinic sees about forty to fifty animals every day. Out of those, I personally inspect fifteen to thirty. Dogs make up at least 75 percent of the practice.

6. The job is very hands-on, day in and day out. For example, I often must hold animals while the doctor performs an exam, or if we have to take x-rays. I also touch the animals whenever I take their temperature or heart rate. And of course, the animals do not always sit still. So the job is always hands-on.

7. About 80 percent of the animals we see are on some sort of flea- or tick-prevention treatment. I have always been concerned about the chemicals in/on those products. Unfortunately, we often have no idea what specific product or brand the pet owner uses at home.

8. Sometimes I will be holding a dog and the owner will say, "Watch out, I put medication on this morning," or I will see a wet spot on its fur where it was recently treated.

9. When I work at the clinic, I sometimes see dogs and cats wearing flea and tick collars. When I take the collars off, my hands often have powder on them.

10. I understand that the EPA has approved the pesticide tetrachlorvinphos (TCVP) for use in flea collars and other pet products. I also understand that these pesticides can be harmful to children and adults when they come into contact with them.

11. I am concerned about the harm to myself and my husband from exposure to TCVP. As a veterinary professional, I strive not to transmit disease or chemical residues between patients, and I make it a habit to wash my hands between patients. But we are often so busy that I do not have time to put on gloves or a gown. During the day, I will have many occasions where I will need to hold a dog or cat in such a way that any residues on their fur will get onto my hands, arms, face, or clothes. And then, when I go home, I may expose my husband to whatever residues are still on me.

12. Personally, I think it is unconscionable that pet products containing TCVP are still allowed on the market, and that the EPA has not resolved NRDC's petition to ban them—especially given the safer and more effective alternatives that are available.

13. In my professional opinion, non-prescription flea collars are not effective and serve no purpose in the veterinary world. I am not aware of any veterinarians that would ever recommend them. There are so many better and safer alternatives out there. In our clinic, we prefer non-topicals and typically recommend oral products instead.

14. EPA's failure to ban TCVP pet products is particularly frustrating for me because, in my personal life, I try to avoid exposure to unsafe pesticides. But then, at work, I risk being exposed to TCVP whether I like it or not. I have no choice but to hold our client's pets, and I do not know whether they have been treated with a TCVP product.

15. My husband and I would benefit if the EPA granted NRDC's petition to ban TCVP pet products, as it would eliminate our risk of exposure to this harmful pesticide. A ban would also benefit my coworkers and our customers and their families.

I declare under penalty of perjury that the foregoing is true and correct, to the best of my knowledge, information, and belief. Executed on April 22, 2019, in Sarasota, Florida.

Diana Owens

Diana Owens

Exhibit D

IN THE UNITED STATES COURT OF APPEALS
FOR THE NINTH CIRCUIT

IN RE NATURAL RESOURCES DEFENSE COUNCIL, INC., *Petitioner*, v. U.S. ENVIRONMENTAL PROTECTION AGENCY, et al., *Respondents*.	Case No. 19-_____

DECLARATION OF MIRIAM ROTKIN-ELLMAN

I, Miriam Rotkin-Ellman, declare as follows:

1. I am a Senior Scientist with the Natural Resources Defense Council ("NRDC"). I received a Master of Public Health from the University of California, Berkeley in 2006 and a Bachelor of Science from Brown University in 2000.

2. I have worked for NRDC's health program since 2006. The program's goals include protecting communities from the substantial adverse health effects caused by exposure to pesticides and other toxic chemicals, such as tetrachlorvinphos ("TCVP").

Human Exposure to Tetrachlorvinphos (TCVP)

3. One of my areas of research is children's exposure to pesticides from the use of household pet products, like those containing TCVP. By virtue of my scientific training, my research, and my knowledge of the pertinent scientific literature, I consider myself an expert on the effects of pesticides, including TCVP, on human health.

4. TCVP belongs to a class of pesticides called organophosphates. Organophosphate pesticides are chemically similar to wartime nerve agents, such as sarin gas, and similarly threaten the functioning of the human nervous system. Organophosphates are highly toxic to the nervous system of both invertebrates (i.e., fleas and ticks) and mammals (i.e., pets and people).

5. TCVP inhibits acetylcholinesterase, an enzyme that breaks down acetylcholine. Acetylcholine is a neurotransmitter which acts as a messenger to stimulate nerves, muscles, the heart, brain, eyes, and glands. When acetylcholine is not broken down by acetylcholinesterase, it builds up, causing overstimulation of the nervous system and leading to the clinical symptoms of poisoning. This "overexcitation" is also the mechanism by which fleas and ticks are killed.

6. Clinical symptoms of human poisoning due to organophosphate pesticides exposure include: eye pupil contraction and tearing, increased salivation, sweating, vomiting, wheezing, dizziness, confusion, seizures, and involuntary urination and defecation. In large doses, these pesticides can harm or kill cats, dogs, and in extreme poisoning cases even humans.

7. Young children's exposure to organophosphates is particularly troubling because their neurological and metabolic systems are still developing. Research indicates additional health effects to children that may occur at even lower levels of exposure and last much longer than the poisoning symptoms. For example, a 2013 literature review found significant evidence, in 26 studies, of adverse neurodevelopmental effects in children linked to organophosphate pesticide exposures. *See* Maria Teresa Munoz-Quezada et al., *Neurodevelopmental Effects in Children Associated with Exposure to Organophosphate Pesticides: A Systematic Review*, 39 Neurotoxicology 158 (2013). Similarly, a 2015 literature review by the U.S. Environmental Protection Agency ("EPA") found that a "growing body of literature" demonstrates that organophosphates "are biologically active

on a number of processes that affect the developing brain." EPA, Literature Review on Neurodevelopment Effects & FQPA Safety Factor Determination for the Organophosphate Pesticides, at 79 (Sept. 15, 2015), *available at* http://tinyurl.com/o8wb6tr.

8. This harm to young children from organophosphate exposure takes the form of reduced cognitive capacity (i.e., lower IQ), delays in motor development, and behavioral problems, including attention deficit/hyperactivity disorder. *See id.* at 80; Munoz-Quezada et al., *Neurodevelopmental Effects in Children*, 39 Neurotoxicology at 160-66; *see also* Maryse F. Bouchard et al., *Attention-Deficit/Hyperactivity Disorder and Urinary Metabolites of Organophosphate Pesticides*, 125 Pediatrics 1270 (2010) (based on national survey data, finding that children with higher organophosphate exposure are more likely to have attention deficit/hyperactivity disorder). These effects may occur at "doses much lower than required to inhibit cholinesterase." James R. Roberts et al., *Pesticide Exposure in Children*, 130 Pediatrics e1765, e1776 (2012).

9. Human exposure to TCVP can occur when children and adults come into contact with a flea collar directly or come into contact

with residues from flea collars. Flea collars are designed to create a coating of the pesticide on the fur of the pet. This residue can be transferred to the skin and clothing of an adult or child during normal contact and play with a pet wearing a flea collar. Once transferred off the pet, people can absorb pesticide residues directly through the skin, and can ingest those residues by touching their hands to their mouth.

10. Children and infants are particularly at risk from exposure to pesticides because their normal activities, such as crawling on the floor and putting their hands in their mouths, can result in increased exposures. For example, a child between the ages of 1 and 2 will put her hands in her mouth nearly 19 times an hour, on average. Jianping Xue et al., *A Meta-Analysis of Children's Hand-to-Mouth Frequency Data for Estimating Nondietary Ingestion Exposure*, 27 Risk Analysis 411, 417 (2007). Children, infants, and fetuses are also particularly at risk because: they take in more pesticides per unit body weight than adults due to their physiology; their neurological and metabolic systems are developing rapidly; and they may have lower capacity to detoxify pesticides. *See* Roberts et al., *Pesticide Exposure in Children*, 130 Pediatrics at e1766.

11. In 2007 and 2008, I conducted a study of the risk of exposure to TCVP residues from flea collars on dog and cat fur. The results of the study were published in the report *Poison on Pets II: Toxic Chemicals in Flea and Tick Collars* (April 2009), https://www.nrdc.org/sites/default/files/poisonsonpets.pdf.

12. In my study, pesticide residues were collected during simulated petting of an animal wearing a TCVP flea collar. Residue levels were analyzed by a commercial laboratory and used to calculate the amount of pesticide a toddler could be exposed to during normal petting and play behavior. Although residue levels varied among the pets in the study, the residue levels were high enough, in many cases, to result in exposures which exceed EPA's safety thresholds for the pesticides.

13. I used similar calculations to translate the TCVP residue levels found in M. Keith Davis et al., *Assessing Intermittent Pesticide Exposure from Flea Collars Containing the Organophosphorus Insecticide Tetrachlorvinphos*, 2008 J. Exposure Sci. & Envtl. Epidemiology 1 (2008), into an estimate of exposure risk. The residue

levels found in the Davis study also translated to exposure that exceeded EPA's safety thresholds.

14. Years later, after EPA analyzed the Davis study and determined that its findings were scientifically sound, and after EPA accounted for its own 2015 literature review on the neurodevelopment effects of organophosphate exposure, EPA issued a human health risk assessment which concluded that interactions with pets treated with TCVP flea collars resulted in potential health risks to young children and occupational handlers (e.g., veterinarians, veterinary assistants, and groomers) that exceeded the agency's level of concern. EPA, TCVP Revised Human Health Risk Assessment, at 9-12, 56-60, 64-69 (Dec. 21, 2016), *available at* https://www.regulations.gov/document?D=EPA-HQ-OPP-2008-0316-0055.

15. Based on the above facts, and my scientific opinion, I am convinced that the use of TCVP in flea collars and pet products poses significant health threats, especially to young children.

NRDC's Petition to Cancel Pet Uses of TCVP

16. On April 23, 2009, NRDC submitted to EPA a petition to cancel all pet uses for tetrachlorvinphos. A copy of *Poison on Pets II* was

submitted to EPA with the petition. The petition also discussed the Davis study.

17. I emailed EPA in November 2013, inquiring about the status of NRDC's petition. EPA did not provide me with a specific date for when the agency expected to answer our petition.

18. In February 2014, NRDC filed a petition for a writ of mandamus in the U.S. Court of Appeals for the D.C. Circuit, seeking an order compelling EPA to respond to NRDC's administrative petition. Only then did EPA act, denying NRDC's petition in November 2014.

19. EPA's justification for denying NRDC's petition in November 2014 was scientifically and legally inadequate. Among other flaws, EPA simply ignored—without explanation—the 2008 Davis study, which was the only peer-reviewed, published study on the subject.

20. NRDC challenged EPA's November 2014 denial in the U.S. Court of Appeals for the Ninth Circuit. Shortly after NRDC filed its opening brief, however, EPA announced that it wanted to reassess the risks posed by the pesticide instead of defending its denial of NRDC's petition. EPA then moved for a voluntary remand.

21. I was concerned that a voluntary remand would lead to further delays. At NRDC, I have also been working on a parallel petition to EPA to ban the use of chlorpyrifos, another organophosphate pesticide that poses serious risks to public health. EPA has repeatedly delayed resolution of NRDC's administrative petition to ban chlorpyrifos, just as it has with TCVP.

22. I had also been tracking EPA's registration review process for TCVP pursuant to section 3(g) of the Federal Insecticide, Fungicide, and Rodenticide Act ("FIFRA"), 7 U.S.C. § 136a(g), and had observed that that process was subject to a number of delays. For example, in November 2008 EPA published a Final Work Plan for the TCVP registration review. The Work Plan is available online at http://tinyurl.com/ncmulgd. The Work Plan included an estimated timeline for completion of the registration review, with a final decision on the registration anticipated by the end of 2014. However, by late 2015, EPA had clearly exceeded that schedule.

23. Concerned about these delays, NRDC asked the Ninth Circuit to ensure that EPA timely resolved NRDC's administrative petition following the voluntary remand by, for example, imposing a

deadline on the agency. However, EPA opposed those requests and stated that it was committed to completing the remanded proceedings within a reasonable time. EPA said that it intended to issue a final, revised response to NRDC's petition within 90 days of finalizing a new risk assessment for TCVP.

24. On December 21, 2016, EPA finalized its new risk assessment and, as discussed above, found potential risks to children and occupational handlers that exceed the agency's level of concern.

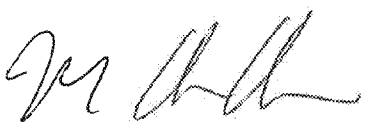
25. On March 21, 2017, 90 days after it finalized its new TCVP risk assessment, EPA did not issue a final revised response to NRDC's cancellation petition. Instead, EPA sent NRDC a short, three-sentence letter, which stated in relevant part: "EPA intends to address any risk-mitigation issues for the pet-care uses of TCVP when it addresses risk-mitigation issues for all TCVP products in the course of registration review for the chemical."

26. At the time, EPA's publicly available 2017 Registration Review Schedule indicated that the agency would issue a proposed interim decision on TCVP's registration between July and September

2017. However, in September 2017, EPA released a new schedule that omitted any reference to TCVP altogether.

27. EPA has since taken no further public action to mitigate the health risks it identified in its TCVP risk assessment, or to resolve NRDC's cancellation petition. Meanwhile, TCVP continues to be sold in household pet products, and to threaten the neurodevelopment of young children who are exposed through their treated pets.

I declare under penalty of perjury that the foregoing is true and correct, to the best of my knowledge, information, and belief. Executed on May 2, 2019, in San Francisco, California.



Miriam Rotkin-Ellman

Exhibit E

PETITION TO CANCEL ALL PET USES FOR THE PESTICIDE TETRACHLORVINPHOS

Filed April 23, 2009

The Natural Resources Defense Council (NRDC) petitions EPA to cancel all pet uses for the pesticide tetrachlorvinphos. This petition is filed pursuant to the Administrative Procedure Act, 5 U.S.C. § 551 et seq.

INTRODUCTION

Tetrachlorvinphos is an insecticide, which belongs to a class of pesticides called organophosphates, which EPA has grouped together based on their common mechanism of toxicity. The devastating effects of this class of pesticides, originally designed as wartime nerve agents including sarin gas, are attributed to their inactivation of an enzyme called cholinesterase.[1] This enzyme is responsible for the timely deactivation of the nerve signaling protein acetylcholine.

Acetylcholine is a messenger of the nervous system, a "neurotransmitter," which carries the signal from a nerve cell to its target. Important targets of acetylcholine include muscles, sweat glands, the digestive system, and even heart and brain cells. In particular, acetylcholine signals activity of the "rest and digest" portions of the nervous system (the parasympathetic system) that stimulates digestion, slows the heart rate, and helps the body to conserve energy. The organophosphate pesticides, including tetrachlorvinphos, block the ability of cholinesterase to deactivate acetylcholine after its message is delivered. The resulting accumulation of acetylcholine causes over-activation of all its targets. Clinical symptoms of organophosphate poisoning can include: eye pupil contraction, increased salivation, nausea, dizziness, confusion, convulsions, involuntary urination and defecation, and, in extreme cases, death by suffocation resulting from loss of respiratory muscle control.

In addition, EPA designated tetrachlorvinphos as "likely to be carcinogenic to humans" in 2002.[2] This designation means that "the weight of the evidence is adequate to demonstrate carcinogenic potential to humans...."[3]

Tetrachlorvinphos was first registered for use in 1966. It was used on crops until 1987. Now, it is primarily used on animals (both livestock and pets) to control flies, mites, and fleas.[4] EPA estimates that 853,000 pounds are used annually on animals. Ten percent of

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[1] As chemical weapons, the production and stockpiling of organophosphate nerve agents are outlawed by the United Nations' 1993 Convention on the Prohibition of the Development, Production, Stockpiling and Use of Chemical Weapons and on Their Destruction. ¶71(b).

[2] U.S. EPA Memorandum, from Jess Rowland to Division Directors, "Chemicals Evaluated for Carcinogenic Potential by the Office of Pesticide Programs," September 24, 2008.

[3] *Id.*

[4] U.S. EPA, Reregistration Eligibility Determination for Tetrachlorvinphos, July, 2006, p. 15. (RED)

households with dogs or cats treat their animals with products containing tetrachlorvinphos.[5] A smaller percentage of animals in other categories are treated with tetrachlorvinphos, including horses (6%), poultry (6%) and beef cattle (2%).[6]

LEGAL STANDARD

EPA regulates pesticides under the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 U.S.C. § 346a, and the Federal Fungicide, Insecticide, and Rodenticide Act (FIFRA), 7 U.S.C. § 136. FIFRA requires that pesticides must be registered to be sold in the United States.[7] EPA may not register a pesticide unless the chemical will perform its intended function without causing any "unreasonable adverse effects on the environment."[8] An unreasonable adverse effect on the environment is an "unreasonable risk to man or the environment, taking into account the economic, social and environmental costs and benefits of the use of any pesticide ...."[9]

The Food Quality Protection Act requires EPA to set the maximum amount of pesticide residue allowed on food – called a "tolerance." As part of the determination for the tolerance, EPA must consider "aggregate exposure" to the pesticide, which includes "all anticipated dietary exposures and all other exposures for which there is reliable information."[10]

REREGISTRATION OF TETRACHLORVINPHOS

Under FIFRA, EPA was required to re-register all pesticide active ingredients that were registered before 1984. An interim risk management decision was made for tetrachlorvinphos in 2002. That decision was finalized in 2006 after EPA completed the cumulative risk assessment for all organophosphate pesticides. As a result, among other things, EPA reregistered the pet collar uses for the pesticide.

As part of the reregistration determination, EPA conducted a preliminary human health risk assessment for tetrachlorvinphos in 1998, which was last revised in 2002.[11] EPA calculated a chronic dietary reference dose (RfD) of 0.0423 mg/kg/day for tetrachlorvinphos, which represents an estimate of "a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime."[12]

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[5] *Id.*

[6] *Id* at 22.

[7] 7 U.S.C. § 136a.

[8] *Id.* § 136a(c)(5)(C).

[9] *Id.* § 136(bb)

[10] 21 U.S.C. § 346a(b)(2)

[11] RED, 23, 24.

[12] RED, 24. EPA Glossary, http://www.epa.gov/economics/children/basic_info/glossary.htm#r

Exposures to doses higher than the RfD are unsafe, especially to sensitive subgroups, such as children and infants. Recognizing the special sensitivities of toddlers, EPA noted, "Although postapplication risks were not determined for adults, toddler exposures represent the worst case due to typical mouthing behaviors and body weight and surface area considerations; therefore, the risk assessment for toddlers is protective of adults."[13]

Based on its risk assessment, EPA determined that tetrachlorvinphos could be reregistered, meaning it can be used in pet collars with the only instruction that the collars be replaced every five months.[14]

EPA FAILED TO CONSIDER PET COLLAR EXPOSURES

In EPA's risk assessment of tetrachlorvinphos, EPA considered the exposures from various residential uses, including uses on pets such as sprays, dips, and powders. However, the agency affirmatively decided not to include pet collar uses because "[p]ost application exposure to residues from pet collars is considered to be insignificant when compared with exposure to other products. Because other, higher exposure uses were not of concern, an assessment for collars was not conducted."[15]

This decision not to assess the exposure from pet collar uses is incongruous with the statement, one page later, about the margin of exposure (MOE), the margin between the no observable adverse effect level and the actual exposure. In finding that the MOE for adult aggregate risks were below the level of concern, EPA did note that "the worst case scenario was collars with an MOE of 240 [for residential handlers]."[16]

Despite finding that pet collar uses provided the highest exposure levels for adults, EPA still chose not to conduct a risk assessment for pet collars. EPA further ignored altogether the possibility that the pet collar uses could expose infants and children to unsafe levels of exposure. The Agency's decision to ignore this source of exposure is arbitrary, capricious, and contrary to law.

EPA USED FAULTY EXPOSURE ASSUMPTIONS

In 2006, NRDC commented that EPA's assumptions about toddlers used in the organophosphate cumulative risk assessment were flawed.[17] Specifically, EPA's risk assessment for pet products significantly underestimated a toddler's exposure to residue on a pet from a flea collar.

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[13] RED, 36.

[14] RED, 64.

[15] RED, 36.

[16] RED, 37.

[17] NRDC comments on the EPA *Organophosphate Cumulative Risk Assessment* (October 2, 2006), EPA docket EPA-HQ-OPP-2006-0618.

First, the tetrachlorvinphos risk assessment assumed that toddlers would have contact with only one treated pet per day, for no more than one hour per day. However, EPA's own assessment of the pesticide dichlorvos (DDVP), which had been used in pet collars, assumed that toddlers were exposed for two hours per day.[18] Furthermore, EPA assumed that the frequency of hand to mouth activities was nine times per hour, but a published review of the scientific literature by EPA scientific experts found that the average frequency of mouthing activities indoors for toddlers between one and two years old is 19.6 times per hour. [19] Both of these assumptions in the tetrachlorvinphos risk assessment are unrealistic, inconsistent with previous agency findings, and tend to significantly underestimate actual risk to toddlers.

EPA also ignored the exposure from toddlers who touch an object or food with pesticide-contaminated hands, and then put that object or food into his/her mouth – that is, indirect hand to mouth activity. However, published studies show that there is actually noticeable indirect hand to mouth activity in infants and children.[20] In fact, one study found that, on average, a toddler will touch an object and then put that object into his or her mouth 15 times in one hour.[21] At the high end of the study's distribution (90th percentile), that rate rises to 66 times per hour. This same study found a statistically significant positive correlation between the frequency of object or food in mouth activity and blood lead levels.

EPA must incorporate the information from these peer-reviewed, published studies in its assessment of the risks associated with pet uses of tetrachlorvinphos.

UNACCEPTABLY HIGH EXPOSURES FROM PET COLLAR USES

Contrary to EPA's decision that risks of exposure from pet collars are "insignificant," testing by NRDC has shown that dangerous levels of tetrachlorvinphos can remain as a detectable residue on a dog or cat's fur for two weeks after the collars are first worn. In the report ""Poison on Pets II: Toxic Chemicals in Flea and Tick Collars," NRDC found that residues of tetrachlorvinphos on the pets' fur were high enough to pose a significant risk to both children and adults who play with their pets.

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[18] EPA Reregistration Eligibility Determination for Dichlorvos (DDVP), July 2006, page 167.

[19] Xue J, et al "Meta-Analysis of Children's Hand-to-Mouth Frequency Data for Estimating Nondietary Ingestion Exposure" 27 Risk Analysis 2 (2007).

[20] Ko, Stephen, Schaefer, Peter D., Vicario, Cristina M., and Binns, Helen J. Relationship of video assessments of touching and mouthing behaviors during outdoor play in urban residential yards to parental perceptions of child behaviors and blood lead levels. *Journal of Exposure Science and Environmental Epidemiology*. 2007 17, 47-57; Reed, KJ, Jiminez, M, Freeman, NCG, and Lioy, PJ. Quantification of children's hand and mouthing activities through a videotaping methodology. *Journal of Exposure Analysis and Environmental Epidemiology*. 1999, 9, 513-520.

[21] Ko, Stephen, Schaefer, Peter D., Vicario, Cristina M., and Binns, Helen J. Relationship of video assessments of touching and mouthing behaviors during outdoor play in urban residential yards to parental perceptions of child behaviors and blood lead levels. *Journal of Exposure Science and Environmental Epidemiology*. 2007 17, 47-57.

NRDC tested the residues of tetrachlorvinphos left on pets after the pet had worn a collar for three days and fourteen days. The pesticide residues were sampled using a protocol based on the methods used by Chambers, et al., which was repeated by Davis, et al. 2008.[22] [23] In NRDC's sampling, residues were collected on microfiber filters moistened with a solution to simulate human perspiration.[24] A rectangular area below the collar and around the pet's shoulders was wiped thoroughly for one minute with the moistened filter to simulate petting. A commercial laboratory analyzed the fur wipe samples using EPA method 8141A.

NRDC then calculated the dose for a toddler between the age of one and two years old, based on exposure parameters taken from published and government agency studies. Because the exposure parameters used by EPA in the tetrachlorvinphos risk assessment were flawed, as described above, NRDC relied on more accurate exposure parameters that reflect a toddler's exposure to a pet and residue on a pet's fur. The exposure assessment included dermal and oral exposure, accounting for both direct hand-to-mouth activity and indirect contact – that is, contact with objects or food that are then placed in the mouth. Because children's behavior with their pets can vary, NRDC evaluated two scenarios that approximate an average and high level of contact with a pet. The average scenario was based on the EPA Standard Operating Procedure for Exposure Assessments and includes a child playing with a pet for two hours, while the high contact scenario reflects eight hours per day, including sleeping, of contact with one or more pets.

Based on these updated parameters and the residues on the tested animals' fur, NRDC calculated that after only three days of wearing a collar 3 out of 5 dogs (60%) and 2 out of 5 cats (40%) had measured residue levels on their fur that were high enough to cause a toddler with average hand-to-mouth behavior and average contact with the contaminated animal to be dosed with tetrachlorvinphos levels up to three times higher than the RfD. That is, the calculated dose from these high residue levels was between 0.09 mg/kg/day and 0.11 mg/kg/day, much higher than the RfD of 0.04 mg/kg/day.

For a toddler with behaviors leading to high exposure to a pet wearing the pet collar, 4 out of 5 dogs (80%) and 5 out of 5 cats (100%) had residue levels high enough to lead to doses above the reference dose. Even after fourteen days of wearing a collar, 2 out of 3 dogs (67%) and 2 out of 2 cats (100%) still had levels of residue so high that toddlers with high-exposure behaviors would be dosed above the RfD. The average dose for these high-exposure behavior kids was 20 times higher than the RfD at three days after the

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[22] Chambers, JE, Boone, JS, Davis, MK, Moran, JE and Tyler JW. 2007. Assessing transferable residues from intermittent exposure to flea control collars containing the organophosphate insecticide chlorpyrifos. *Journal of Exposure Science and Environmental Epidemiology*, 17(7): 656–666.

[23] Davis, MK, Boone, JS, Moran JE, Tyler, JW and Chambers JE. 2008. Assessing intermittent pesticide exposure from flea control collars containing the organophosphorus insecticide tetrachlorvinphos. *Journal of Exposure Science and Environmental Epidemiology,* advance online publication, 1-7.

[24] Surfactant solution used to simulate human perspiration in California EPA DPR Guidance for Determination of Dislodgeable Foliar Residue. Worker Health and Safety Branch, Health and Safety Report HS-1600. Revision February 20, 2002.

collar is applied (with the peak dose of 1.74 mg/kg/day from one cat), and three times higher at 14 days after the collar is applied.

The maximum residue measured by the only other study of tetrachlorvinphos residues from flea collars (the "Davis study") greatly exceeds the residues measured by NRDC.[25] It was measured as a result of petting at the neck with the collar in place for five minutes on day seven after application of the collar. By comparison, the NRDC sampling protocol involved petting the animal for one minute in an area behind and not touching the collar on the third day. Using EPA exposure assessment methods, this residue level is approximately 150 times the RfD. Using NRDC's high end exposure assessment this residue level is approximately 4,000 times the RfD.

The Davis study also calculated the average residue level measured at the neck with the collar, at the neck without the collar, and in the tail region over 112 days. Using EPA exposure methods, this residue level is approximately 90, 27, and 1 times the RfD respectively. Using NRDC's high end exposure assessment this residue level is approximately 2,500, 770, and 23 times the RfD, respectively.

EPA's failure to provide any calculations of the risks from exposure to pet collars in its risk assessment for the reregistration eligibility determination renders that determination arbitrary and capricious, and contrary to law. Flea collar uses alone have been shown to exceed the health-based reference dose. EPA completely ignored the risk from these types of exposures in the residential risk assessment which affects the determination about whether to reregister tetrachlorvinphos. As a result, the eligibility determination is fatally flawed.

The residue levels found on pets at three days and fourteen days of wearing a flea collar exceed the safe doses allowable by EPA. However, these residue levels were never considered in the tetrachlorvinphos risk assessment. As a result, EPA improperly permitted the continued use of tetrachlorvinphos in pet collars, which has left toddlers living with pets wearing these flea collars exposed to dangerous levels of a toxic pesticide. In light of EPA's failure to assess the risk from pet collars, its use of improper exposure parameters in the risk assessment that was conducted, and the Poison on Pets II findings that toddlers living with pets wearing flea collars are routinely exposed to levels of tetrachlorvinphos that exceed the reference dose, EPA must exercise its statutory obligation to protect children by canceling all pet uses of tetrachlorvinphos.

Respectfully submitted,

Gina Solomon, MD, MPH
Mae Wu, Esq.
Natural Resources Defense Council

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[25] Davis, MK, Boone, JS, Moran JE, Tyler, JW and Chambers JE. 2008. Assessing intermittent pesticide exposure from flea control collars containing the organophosphorus insecticide tetrachlorvinphos. *Journal of Exposure Science and Environmental Epidemiology,* advance online publication, 1-7.

Exhibit F

No. 14-1017

IN THE UNITED STATES COURT OF APPEALS
FOR THE DISTRICT OF COLUMBIA CIRCUIT

IN RE NATURAL RESOURCES DEFENSE COUNCIL, INC.,
PETITIONER

On Amended Petition for a Writ of Mandamus and for Relief from Unreasonably Delayed Agency Action by the Environmental Protection Agency

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AMENDED BRIEF FOR PETITIONER

Dimple Chaudhary
Natural Resources Defense Council
1152 15th Street, NW, Suite 300
Washington, D.C. 20005
(202) 717-8234
dchaudhary@nrdc.org

Counsel for Petitioner

Dated: April 8, 2014

INTRODUCTION

This amended petition for a writ of mandamus seeks an order requiring the U.S. Environmental Protection Agency (EPA) to respond to petitioner Natural Resources Defense Council's (NRDC's) petition to cancel the use of the pesticide tetrachlorvinphos in flea collars and other pet products.[1] In its petition and supporting documentation, NRDC presented evidence to EPA that toddlers may be exposed to residues from flea collars containing tetrachlorvinphos in amounts that exceed the levels EPA has found to be safe. EPA has failed to answer NRDC's petition for almost five years, leaving potentially millions of children, adults, and pets at risk of exposure to unsafe levels of this dangerous pesticide. The Court should order EPA to respond.

[1] On February 6, 2014, NRDC filed a petition for writ of mandamus in this Court seeking an order compelling EPA to respond to NRDC's petition to cancel pet uses of tetrachlorvinphos, as well as to respond to a separate NRDC petition seeking cancellation of pet collar uses of the pesticide propoxur. *See* Doc. No. 1478697. On March 26, 2014, EPA published a final order cancelling all pet collar uses of propoxur. Product Cancellation Order for Certain Pesticide Registrations, 79 Fed. Reg. 16,793 (Mar. 26, 2014). Accordingly, NRDC withdraws its petition for writ of mandamus to compel a decision on its propoxur cancellation petition, and submits this amended petition for writ of mandamus only with regards to its tetrachlorvinphos petition. This amended petition omits discussion of NRDC's propoxur petition, and contains no other material changes.

STATEMENT REGARDING ADDENDA

Relevant statutes and regulations, and supporting declarations and exhibits, were submitted on February 6, 2014 with the originally filed petition for writ of mandamus as separate addenda, Document No. 1478697.

STATEMENT OF JURISDICTION AND APPLICABLE LAW

NRDC submitted a petition to EPA in 2009 pursuant to the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), 7 U.S.C. §§ 136 *et seq.*, and the Administrative Procedure Act (APA), 5 U.S.C. §§ 500 *et seq.*, seeking cancellation of all pet uses for the pesticide tetrachlorvinphos.[2] This is a challenge to EPA's failure to respond to NRDC's petition.

This Court has jurisdiction to hear NRDC's request for a writ of mandamus under the APA. The APA provides that "[a] person suffering legal wrong because of agency action, or adversely affected or aggrieved by agency action within the meaning of a relevant statute, is entitled to judicial review thereof." 5 U.S.C. § 702. A federal agency is obligated to "conclude a matter" presented to it "within a reasonable time," *id.* § 555(b), and a reviewing court may "compel agency action unlawfully withheld or unreasonably delayed." *Id.* § 706(1).

[2] The petition is included in Petitioner's Supplemental Materials addendum, attached to the Declaration of Miriam Rotkin-Ellman as Exhibit N. All references to supplemental materials can be found in the addenda filed with Petitioner's original petition, Document No. 1478697.

Where review of final agency action is committed by statute to a U.S. court of appeals, jurisdiction to review agency inaction also lies exclusively with the same courts. *Telecomm. Research & Action Ctr. (TRAC) v. FCC*, 750 F.2d 70, 75 (D.C. Cir. 1984). Here, the courts of appeals have jurisdiction to review any final action by EPA under FIFRA. The statute provides the courts of appeals with "exclusive jurisdiction" to review "the validity of any order issued by the Administrator following a public hearing." 7 U.S.C. § 136n(b). The Ninth Circuit has held that the opportunity for submission of written comments constitutes such a "public hearing." *See United Farm Workers of Am. v. Adm'r, EPA*, 592 F.3d 1080, 1082 (9th Cir. 2010); *cf. Envtl. Def. Fund, Inc. v. Costle*, 631 F.2d 922, 926, 932 (D.C. Cir. 1980) (a "public hearing" pursuant to Section 136n(b) does not require oral presentation of arguments to an agency decision-maker).

NRDC submitted an administrative petition to EPA with written arguments for cancelling pet uses of tetrachlorvinphos. The Agency published notice of NRDC's petition in the *Federal Register* and solicited public comments. *See* Petition Requesting Cancellation of all Tetrachlorvinphos Pet Uses and Extension of Comment Period for Petition Requesting Cancellation of Propoxur Pet Collar Uses; Notice of Availability, 74 Fed. Reg. 27,035 (Jun. 5, 2009). This process satisfies FIFRA's public hearing requirement and creates a suitable record for appellate review. *See United Farm Workers of Am.*, 592 F.3d at 1082-83. Thus,

because the Court would have jurisdiction to review any final action taken by EPA in response to NRDC's petition, the Court also has jurisdiction to review this challenge to EPA's failure to respond to the petition.

The Court has the authority to issue a writ of mandamus requiring EPA to respond to NRDC's petition under the All Writs Act, 28 U.S.C. § 1651(a). The All Writs Act provides that "[t]he Supreme Court and all courts established by Act of Congress may issue all writs necessary or appropriate in aid of their respective jurisdictions and agreeable to the usages and principles of law." *Id.*

STATEMENT OF THE ISSUE PRESENTED FOR REVIEW

Whether, after receiving a petition to cancel pet uses for the pesticide tetrachlorvinphos that pose unreasonable adverse risks to human health, EPA's failure to respond for almost five years is an unreasonable delay such that this Court should order the Agency to respond?

STATUTORY FRAMEWORK

EPA oversees pesticide regulation under FIFRA. FIFRA requires pesticides to be registered prior to sale or distribution in the U.S. 7 U.S.C. § 136a(a). EPA may register a pesticide only if it will "perform its intended function" without causing "unreasonable adverse effects on the environment." *Id.* § 136a(c)(5)(C). A pesticide causes unreasonable adverse effects on the environment if it poses "any unreasonable risk to man or the environment, taking into account the economic,

social, and environmental costs and benefits of the use of any pesticide." *Id.* § 136(bb). The Administrator may cancel the registration of any pesticide that causes unreasonable adverse effects on the environment. *Id.* § 136d(b)(1).

FIFRA was amended in 1988 to require the reregistration of pesticides containing an active ingredient that was first registered prior to November 1, 1984. Pub. L. No. 100-532, 102 Stat. 2554 (1988) (codified at 7 U.S.C. § 136a-1(a)). As part of the reregistration process, EPA reviewed the scientific data underlying a pesticide's registration, including an assessment of human health and ecological risks. See 7 U.S.C. § 136a-1(b)-(g). The results of EPA's reviews were published in Reregistration Eligibility Decisions for each pesticide. *See, e.g.,* Reregistration Eligibility Decision for Tetrachlorvinphos (2006) [hereinafter Tetrachlorvinphos RED].[3] FIFRA required EPA to complete its reregistration of all pesticides by October 3, 2008. 7 U.S.C. § 136a-1(g). Following reregistration, EPA must conduct a periodic review of each pesticide's registration—referred to as "registration review"—every 15 years. 7 U.S.C. § 136a(g).

FACTUAL BACKGROUND

Tetrachlorvinphos is a pesticide currently used in collars, dips, powders, and aerosol and pump sprays to control fleas and ticks. Tetrachlorvinphos RED at 15.

[3] Petitioner's Supplemental Materials, Chaudhary Decl., Ex. B. This document incorporates and finalizes a 2002 Interim Tolerance Reassessment Eligibility Decision for tetrachlorvinphos issued by EPA. For ease of reference, this petition refers to the full document as "Tetrachlorvinphos RED."

Tetrachlorvinphos belongs to a class of pesticides called organophosphates. Rotkin-Ellman Decl. ¶ 6. These pesticides are chemically similar to wartime nerve agents, such as sarin gas, and interact similarly with the human nervous system. *Id.* EPA designated tetrachlorvinphos as "likely to be carcinogenic to humans" in 2002. EPA Memorandum from Jess Rowland to Division Directors, Chemicals Evaluated for Carcinogenic Potential by the Office of Pesticide Programs 19 (Sept. 24, 2008).[4]

Tetrachlorvinphos, as an organophosphate pesticide, interferes with an essential enzyme, acetylcholinesterase, that normally controls messaging between nerve cells. Rotkin-Ellman Decl. ¶ 7. The result of exposure is spasmodic overstimulation of the nervous system; this is the mechanism by which fleas and ticks are killed. *Id.* In large doses, exposure to tetrachlorvinphos can harm or kill cats, dogs, and in extreme poisoning cases even humans. *Id.* ¶ 8. At lower levels, exposure can cause a variety of poisoning symptoms, including eye pupil contraction and tearing, increased salivation, sweating, dizziness, and confusion. *Id.* More severe poisoning can cause involuntary urination and defecation, vomiting, and seizures. *Id.*

Flea collars are designed to create a coating of the pesticide on the fur of a pet. *Id.* ¶ 10. Accordingly, exposure to tetrachlorvinphos primarily occurs when

[4] Petitioner's Supplemental Materials, Chaudhary Decl., Ex. D.

children or adults come into contact with treated flea collars directly, or come into contact with pesticide residues on pets from the flea collars.[5] *Id.* These residues also can be transferred to the skin and clothing of an adult or child during normal contact and play with a pet wearing a flea collar. *Id.*; *see also* Davis et al., *Assessing Intermittent Pesticide Exposure from Flea Collars Containing the Organophosphorus Insecticide Tetrachlorvinphos,* J. of Exposure Sci. & Envt'l Epidemiology (2008) [hereinafter Miss. State Univ. Study].[6] Once transferred off of the pet, people can absorb tetrachlorvinphos residues through their skin and ingest them by touching their hands to their mouth. Rotkin-Ellman Decl. ¶ 10.

Children are particularly at risk from exposure to tetrachlorvinphos because their neurological and metabolic systems are still developing. *Id.* ¶ 11. Recent research indicates that low-level prenatal and early life exposure to this type of pesticide can impair children's neurological development, which can result in pervasive disorders that may include delays in motor development and attention deficit/hyperactivity disorder. *Id.* ¶ 9. Children—especially toddlers—are also more likely than adults to put their hands and other objects in their mouths, and so are more likely to ingest residues of pesticides with which they come into contact. *Id.* ¶ 11.

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[5] Exposure to tetrachlorvinphos can also occur when individuals mix, load, or apply other tetrachlorvinphos-containing flea-control products to their pets, or when they enter or contact treated sites. Tetrachlorvinphos RED at 26.

[6] Petitioner's Supplemental Materials, Rotkin-Ellman Decl., Ex. K.

Exposure to tetrachlorvinphos is widespread. EPA estimates that ten percent of households with dogs or cats treat their animals with products containing tetrachlorvinphos. Tetrachlorvinphos RED at 15. A 2008 study of the residue levels from tetrachlorvinphos-treated flea collars estimated that there are potentially "millions of children who could be in direct contact" with pesticides in flea collars, merely from contact with their dogs. Miss. State Univ. Study at 1.

Although widely used, flea collars are regarded by veterinarians as ineffective. Stone Decl. ¶ 9. Many alternatives, such as oral tablets or less toxic treatments, exist on the market to control fleas and ticks. Rotkin-Ellman Decl. ¶ 13.

PROCEDURAL HISTORY

Tetrachlorvinphos was first registered for use as a pesticide in 1966, and originally used on vegetables, feed crops, livestock, pets, and around buildings. Tetrachlorvinphos RED at 19. Crop uses were voluntarily cancelled in 1987. *Id.* Today tetrachlorvinphos is primarily used to control flies, larvae, and mites in livestock. *Id.* at 15. It is also still allowed in pet products such as flea dips, powders, aerosol and pump sprays, and collars. *Id.*

EPA issued its most recent reregistration eligibility decision for tetrachlorvinphos in July of 2006. *Id.* at cover page. As part of this decision, EPA evaluated exposure to children and adults after an initial pesticide application from various residential uses of tetrachlorvinphos on pets, including sprays, dips, and

powders, and compared those exposures with levels EPA has found to be safe. *Id.* at 36. EPA did not evaluate post-application exposure to residues from pet collar uses because EPA considered it "to be insignificant when compared with exposure to other products." *Id.* In declining to evaluate post-application exposure to pet collars, EPA ignored evidence that such exposure could be significant. *Id.* at 37 (finding that the "worst case" scenario for adult aggregate risk was exposure to pet collars). Based on its assessment, EPA determined that tetrachlorvinphos could be reregistered, including for use in pet products.

In 2008, researchers from the Center for Environmental Health Sciences at Mississippi State University published a study assessing children and adults' exposure to tetrachlorvinphos from the use of a tetrachlorvinphos-formulated collar on a pet dog. *See* Miss. State Univ. Study at 1-2. The study concluded that significant amounts of tetrachlorvinphos residue are transferred from pets to skin and clothing, indicating potential sources of exposure. *Id.* at 6.

In 2007 and 2008, NRDC conducted a study of a toddler's exposure to tetrachlorvinphos due to residues from flea collars containing the pesticide. NRDC, *Poison on Pets II: Toxic Chemicals in Flea and Tick Collars* (April 2009) [hereinafter *Poison on Pets II*].[7] NRDC tested the residues of tetrachlorvinphos on pets' fur after the pets had worn a collar for three days and fourteen days. *Id.* at 7.

[7] Petitioner's Supplemental Materials, Rotkin-Ellman Decl., Ex. A.

Using EPA's exposure assessment methods and other parameters from the published literature, NRDC then calculated the potential dose to toddlers: how much of these residues could be ingested and absorbed through the skin, for an average toddler playing with their pet. *Id.* at 7-8. NRDC found some residue levels translated to exposures at more than twice the level EPA has found to be safe. *Id.* at 9-10.

On April 23, 2009, NRDC filed a petition with EPA to cancel all pet uses for tetrachlorvinphos. NRDC, *Petition to Cancel All Pet Uses for the Pesticide Tetrachlorvinphos* (April 23, 2009) [hereinafter NRDC Tetrachlorvinphos Petition].[8] NRDC highlighted the results of its own exposure study, and further noted that EPA's 2006 risk assessment employed flawed assumptions to underestimate toddlers' exposure to flea collar residue. *Id.* at 3-6. Using EPA's exposure assessment methods, NRDC also calculated that the residue levels found by the Mississippi State University Study translated to exposures for an average toddler up to 150 times higher than the level EPA had found was safe. *Id.* at 6. EPA published a notice of NRDC's petition in the *Federal Register* on June 7, 2009, providing for a sixty-day comment period. Petition Requesting Cancellation of all Tetrachlorvinphos Pet Uses and Extension of Comment Period for Petition Requesting Cancellation of Propoxur Pet Collar Uses, 74 Fed. Reg. at 27,035.

[8] Petitioner's Supplemental Materials, Rotkin-Ellman Decl., Ex. N.

It has now been nearly five years since NRDC filed its petition, and EPA has still not provided any response.

SUMMARY OF ARGUMENT

EPA has a statutory duty under the APA to respond without unreasonable delay to NRDC's petition for cancellation of pet uses for tetrachlorvinphos. Almost five years have now passed since NRDC filed its tetrachlorvinphos petition. Regardless of whether EPA grants or denies this petition, NRDC has a right to a determination of the issues it presented to the Agency. In the case of a denial of the petition, NRDC is entitled to seek further relief from the Agency and the Court, but it cannot exercise those rights until EPA acts. A writ of mandamus is the only remedy that will adequately cure the injury NRDC members have suffered and continue to suffer as a result of EPA's ongoing delay. The harm caused by exposure of NRDC members to tetrachlorvinphos provides ample justification for granting a writ of mandamus under the six factors identified by this Court in *TRAC v. FCC*.

STANDING

NRDC's standing to seek a writ of mandamus is based on the procedural injury the organization has suffered while trying to protect the underlying health interests of its members.

A party suffers a cognizable procedural injury when an agency fails to follow a statutorily mandated procedure if that procedure has the potential to change the agency's mind in a particular matter. *See Lemon v. Geren*, 514 F.3d 1312, 1315 (D.C. Cir. 2008) ("[P]laintiffs suffer harm from the agency's failure to follow [the National Environmental Policy Act's] procedures, compliance with which might have changed the agency's mind[.]"). Additionally, organizations suing for redress of a procedural injury must show that such redress will relieve a concrete underlying harm. *See Lujan v. Defenders of Wildlife*, 504 U.S. 555, 573 n.8 (1992) ("We do *not* hold that an individual cannot enforce procedural rights; he assuredly can, so long as the procedures in question are designed to protect some threatened concrete interest of his that is the ultimate basis of his standing."). NRDC satisfied both parts of this standard.

First, NRDC's petition has the potential to change EPA's position regarding the use of tetrachlorvinphos in flea collars and other pet products.

Second, EPA's failure to respond to NRDC's petition has caused NRDC's members an ongoing injury that only a writ of mandamus from this Court can remedy. NRDC is an environmental and public health organization with approximately 330,000 members nationwide. Lopez Decl. ¶¶ 4-6. NRDC's organizational priorities include reducing and eliminating members' exposures to dangerous chemicals. *Id.* ¶ 6.

NRDC's members include parents of young children who come into contact with pets and are concerned about the effects of tetrachlorvinphos on their children's health. Louchheim Decl. ¶¶ 8-10; Stone Decl. ¶¶ 10-13. NRDC's members also include veterinarians who come into contact with pets wearing flea collars through their professional work, and who are concerned about transferring residues from these collars to their hands and clothing, and ultimately to their children. Stone Decl. ¶¶ 4, 7-8, 12. Exposure of children to pesticides like tetrachlorvinphos is particularly troubling because their neurological and metabolic systems are still developing. Rotkin-Ellman Decl. ¶ 11. Parents who are aware of such risks are nevertheless unable to protect themselves and their children because they cannot know if a particular pet they or their child comes into contact with is wearing (or has recently worn) a tetrachlorvinphos-treated flea collar. Louchheim Decl. ¶¶ 9-10. They also cannot always control whether their child touches or interacts with treated pets, or objects with which those pets come into contact. *Id.* ¶¶ 5-7; Stone Decl. ¶ 12. A writ of mandamus compelling the EPA to take final action would redress the harm suffered by NRDC members who seek a decision on NRDC's petition, and EPA's withdrawal of its approval for pet uses of tetrachlorvinphos.

NRDC also satisfies the requirements for organizational standing. *See Hunt v. Wash. State Apple Adver. Comm'n*, 432 U.S. 333, 343 (1977). Under *Hunt*'s

three-part test, NRDC has standing to sue because: (1) NRDC's "members would otherwise have standing to sue in their own right" because of the injuries described above; (2) the interests NRDC seeks to protect "are germane to the organization's purpose"; and (3) "neither the claim asserted nor the relief requested requires the participation of individual members in the lawsuit." *Id.*

ARGUMENT

I. A Writ of Mandamus Is the Only Remedy that Will Adequately Enforce EPA's Duty to Answer the Petition

The facts of this case satisfy the three-part threshold test for granting a writ of mandamus. A court may grant mandamus relief "if (1) the plaintiff has a clear right to relief; (2) the defendant has a clear duty to act; and (3) there is no other adequate remedy available to plaintiff." *N. States Power Co. v. U.S. Dep't of Energy*, 128 F.3d 754,758 (D.C. Cir. 1997) (internal quotation marks omitted). "The party seeking mandamus has the burden of showing that its right to issuance of the writ is clear and indisputable." *Id.* (internal quotation marks omitted).

Here, EPA has a clear duty to respond to NRDC's petition, and NRDC has a clear right to relief. The APA requires that a petition submitted to an agency be decided by the agency within a reasonable time. *See* 5 U.S.C. § 555(b). NRDC, moreover, has no other remedy available. Without agency action on NRDC's petition, NRDC cannot exercise its right to judicial review. In view of EPA's

extraordinary delay, a writ of mandamus requiring EPA's compliance with the APA is appropriate.

II. A Writ of Mandamus Is Justified under the Equitable Factors Established in *TRAC*

In judging whether a writ of mandamus is necessary to compel agency action in the face of unreasonable delay, this Court has established a flexible, six-factor test: (1) the time agencies take to act is subject to a rule of reason; (2) a statutory scheme may supply the rule of reason; (3) "delays that might be reasonable in the sphere of economic regulation are less tolerable when human health and welfare are at stake"; (4) the court should consider the effect of mandamus on competing agency priorities; (5) the court should consider the nature and extent of the interests harmed by agency delay; and (6) the agency need not be acting in bad faith for its delay to be unreasonable. *TRAC*, 750 F.2d at 80. The balance of factors here supports the conclusion that EPA's delay warrants mandamus.

A. EPA's Delay Is Unreasonable

The "first and most important factor" in assessing the reasonableness of an agency's delay is that the time the agency takes to make a decision "must be governed by a rule of reason. *In re Core Commc'ns, Inc.*, 531 F.3d 849, 855 (D.C. Cir. 2008) (internal quotation marks omitted). In this case, it has been almost five years since NRDC filed its petition requesting that EPA cancel all pet uses for

tetrachlorvinphos. EPA has still not issued a decision on the petition. This delay is unreasonable.

A reasonable time for an agency to respond to a petition "is typically counted in weeks or months, not years." *In re Am. Rivers & Idaho Rivers United*, 372 F.3d 413, 419 (D.C. Cir. 2004). "[E]xcessive delay saps the public confidence in an agency's ability to discharge its responsibilities . . . . [, and] may undermine the statutory scheme and could inflict harm on individuals in need of final action." *Cutler v. Hayes*, 818 F.2d 879, 896-97 (D.C. Cir. 1987). This Court has previously found that an agency delay of three years in granting or denying a petition was unacceptable where human health was at risk. *See Pub. Citizen Health Research Grp. v. Auchter*, 702 F.2d 1150, 1154, 1157 (D.C. Cir. 1983) (noting that "a more than three-year span from [the] petition to projected final regulation is not tolerable" and constitutes "agency action unreasonably delayed").

The reasonableness of the agency's delay must also "be judged in the context of the statute which authorizes the agency's action." *Id.* at 1158 n.30 (internal quotation marks omitted). One of the principal purposes of FIFRA is to keep off the market pesticides whose adverse effects on human health and the environment outweigh any benefits. *See* 7 U.S.C. §§ 136a(c)(5)(C), 136d(b); *Ferebee v. Chevron Chem. Co.*, 736 F.2d 1529, 1540 (D.C. Cir. 1984). Flea collars are regarded by veterinarians as ineffective. Stone Decl. ¶ 9. At the same time,

exposure to tetrachlorvinphos-treated flea collars poses a significant public health threat to humans and pets that come into contact with their chemical residues. *Poison on Pets II* at 4. Delay thus contravenes the intent of FIFRA to keep unsafe and ineffective products like these collars off the market.

EPA has provided no response at all to NRDC's tetrachlorvinphos petition, nor has the Agency provided a specific date when it expects to respond. Rotkin-Ellman Decl. ¶ 23. EPA's ongoing delay in deciding NRDC's petition is unreasonable.

B. EPA's Delay Is Unreasonable Even in the Absence of a Statutory Deadline

Although FIFRA contains no specific deadline for responding to a petition to revoke uses of a pesticide, EPA cannot play "administrative keep-away" interminably by refusing to grant or deny NRDC's petition. *In re Am. Rivers & Idaho Rivers United*, 372 F.3d at 420. In the absence of a statutory deadline, EPA's obligation under the APA to "conclude a matter" presented to it "within a reasonable time" still applies. 5 U.S.C. § 555(b); *see also In re Am. Rivers & Idaho Rivers United*, 372 F.3d at 418.

This Court has repeatedly found agency delay to be unreasonable under the APA notwithstanding the lack of a statutory deadline for agency action. *See In re Am. Rivers & Idaho Rivers United*, 372 F.3d at 419 (finding six-year delay "egregious"); *In re Int'l Chem. Workers Union*, 958 F.2d 1144, 1150 (D.C. Cir.

1992) (finding six-year delay an "extraordinarily long time"); *Auchter*, 702 F.2d at 1154 (finding three-year delay unreasonable). EPA has failed to give NRDC any decision for almost five years on NRDC's tetrachlorvinphos petition. By any standard, EPA's delay is unreasonable.

C. EPA's Delay Affects Human Health and Welfare

EPA's delay is particularly intolerable because it impacts human health and welfare. *See Auchter*, 702 F.2d at 1157-58; *Core Commc'ns*, 531 F.3d at 855. "Delays that might be altogether reasonable in the sphere of economic regulation are less tolerable when human lives are at stake. This is particularly true when the very purpose of the governing Act is to protect those lives." *Auchter*, 702 F.2d at 1157-58 (citations omitted).

Here, a principal purpose of FIFRA is to protect the public from "unreasonable risk" from pesticide exposure. *See* 7 U.S.C. § 136(bb). NRDC has presented EPA with two studies showing that tetrachlorvinphos residue can easily be transferred to the skin or clothing of children and adults while petting or playing with a flea-collar-wearing pet. NRDC Tetrachlorvinphos Petition (citing Miss. State Univ. Study). Once transferred off a pet, these residues can then be absorbed through the skin or ingested, resulting in harmful exposure levels. Rotkin-Ellman Decl. ¶ 10. High levels of exposure to pesticides like tetrachlorvinphos can cause symptoms of poisoning. *Id.* ¶ 8. But more perniciously, low levels of exposure can

quietly impair children's neurological development, and may result in disorders including delays in motor development and attention deficit/hyperactivity disorder. *Id.* ¶ 9. And not only are young children more susceptible to the dangerous effects of tetrachlorvinphos, young children can have higher levels of exposure because they are more likely to ingest residues with which they come into contact. *Id.* ¶ 11.

NRDC has presented unrefuted evidence that tetrachlorvinphos-formulated collars pose risks that exceed EPA's safety threshold. *See Poison on Pets II* at 9-11. These risks of exposure are not limited to those who chose to buy flea collars. For example, NRDC members include veterinarians who frequently interact with pets, but who cannot control whether those pets have recently worn tetrachlorvinphos-treated flea collars. Stone Decl. ¶¶ 7-8. NRDC members also include parents of young children who cannot always control whether their child comes into contact with a pet that has recently worn a flea collar. Louchheim Decl. ¶¶ 6-7, 9. Given these risks, NRDC members are justifiably concerned about their own exposure and their children's exposure to tetrachlorvinphos. Louchheim Decl. ¶ 10; Stone Decl. ¶ 12. The inability of these individuals to eliminate or reduce the hazards presented by treated flea collars compounds the unreasonableness of EPA's delay. *Cutler*, 818 F.2d at 898.

Instead of issuing a decision on NRDC's petition, EPA has left health risks unabated in the face of compelling evidence that pet uses of this dangerous pesticide should be cancelled. The Court should not permit further delay.

D. No Competing Priorities Justify EPA's Delay

Federal agencies invariably face the challenge of limited resources with which to address competing priorities. *See id.* at 896. Here, however, EPA has not cited competing priorities that would limit its ability to respond to NRDC's petition. In light of the amount of time that has passed since NRDC submitted its petition, any justifications EPA now raises concerning competing agency priorities have lost force. *Id.*, 818 F.2d at 898 (explaining that an agency's "justifications [for delay] become less persuasive as delay progresses"); *see also Muwekma Tribe v. Babbitt*, 133 F. Supp. 2d 30, 40 (D.D.C. 2000) (noting that the D.C. Circuit has found extensive delays are unacceptable notwithstanding competing interests).

The scope of NRDC's petition is modest: NRDC has requested cancellation of one type of use for one pesticide. NRDC has submitted compelling evidence that pet uses of this pesticide exceeds EPA's own safety threshold. EPA has had ample time to consider any scientific or technical issues raised by NRDC's petition. EPA's justification for its delay, moreover, must be "balanced against the potential for harm." *Cutler*, 818 F.2d at 898. In this case, EPA's delay has resulted

in ongoing exposure to unsafe levels of a toxic pesticide. This harm clearly outweighs any justification for delay.

E. The Harm Caused by EPA's Delay Is Serious and Wide-Ranging

The nature and extent of the interests harmed by agency delay also weigh heavily in favor of a writ of mandamus. EPA's failure to respond to NRDC's petition only perpetuates the underlying harm suffered by NRDC members through exposure to tetrachlorvinphos. Until EPA decides NRDC's petition and withdraws approval of the use of tetrachlorvinphos in pet products, NRDC's members and their children will continue to be exposed to this harmful pesticide. *See* Louchheim Decl. ¶¶ 8-10; Stone Decl. ¶¶ 6-8, 12-13.

The prevalence of tetrachlorvinphos-treated flea collars means that exposure is wide-ranging. Tetrachlorvinphos RED at 15. Potentially millions of children and adults may be exposed to harmful levels of this pesticide simply by hugging, petting, and playing with their pet. Miss. State Univ. Study at 1. And as discussed above, numerous scientific studies have established that exposure to this type of pesticide poses serious risks, especially to young children. *See supra* II.C. The Court should order EPA to act in light of the serious and wide-ranging harm posed by tetrachlorvinphos.

NRDC's interest in challenging the registration of tetrachlorvinphos is also prejudiced by delay. Without a final decision on its petition, it cannot challenge the

merits of EPA's decision to allow this dangerous pesticide to remain on the market. The Court should not permit EPA to skirt challenges to this decision by endlessly delaying final action. *Cf. Am. Broad. Co. v. FCC*, 191 F.2d 492, 501 (D.C. Cir. 1951) ("Agency inaction can be as harmful as wrong action. The [agency] cannot, by its delay, substantially nullify rights which the [statute] confers, though it preserves them in form.").

F. The Court Need Not Find EPA Acted in Bad Faith

The Court "need not find any impropriety lurking behind agency lassitude in order to hold that agency action is unreasonably delayed." *TRAC*, 750 F.2d at 80 (internal quotation marks omitted). NRDC has no evidence that EPA is acting in bad faith. But EPA has failed for almost five years to provide any response to NRDC's petition. Whether based on bad faith or extreme inattention, the Court should find that EPA acted and has continued to act with unreasonable delay.

CONCLUSION

EPA's failure to respond for almost five years to NRDC's tetrachlorvinphos petition is unreasonable in light of the serious, wide-ranging harm caused by exposure to this pesticide. NRDC respectfully requests that this Court order EPA to respond to NRDC's petition within sixty days by either denying the petition or issuing a responsive rulemaking.

Dated: April 8, 2014

By: /s/ Dimple Chaudhary
Dimple Chaudhary

Exhibit G

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

CERTIFIED MAIL

November 6, 2014

Miriam Rotkin-Ellman
Gina Solomon, MD, MPH
Mae Wu, Esq.
Natural Resources Defense Council
111 Sutter Street, 20th Floor
San Francisco, CA 94104

Re: Response to Natural Resources Defense Council's April 23, 2009 Petition Requesting Cancellation of All Pet Uses of Tetrachlorvinphos

Dear Ms. Rotkin-Ellman, Dr. Solomon, and Ms. Wu:

This letter constitutes the Environmental Protection Agency's (EPA or the Agency) response to the Natural Resources Defense Council's (NRDC) petition dated April 23, 2009 (Petition) requesting that EPA cancel all pet uses of the pesticide tetrachlorvinphos (TCVP). For the reasons identified below, the Agency denies NRDC's request to cancel all pet uses of TCVP.

The Petition asserts that EPA's revised human health risk assessment and organophosphate (OP) cumulative risk assessment underlying EPA's 2006 Reregistration Eligibility Decision (RED) for TCVP failed to adequately assess residential exposures to pet collars, and also presents NRDC's April, 2009 "Issue Paper" entitled "Poisons on Pets II: Toxic Chemicals in Flea and Tick Collars." The Petition concludes that EPA's 2006 RED for TCVP is "arbitrary and capricious, and contrary to law," and that "EPA must … cancel all pet uses of [TCVP]." Petition at 6. As explained below, in response to NRDC's Petition, EPA has conducted an updated non-occupational residential exposure assessment for all TCVP pet product uses. Based on that assessment, EPA does not find risks of concern resulting from pet uses of TCVP and therefore declines today to initiate cancellation action against such uses as requested in the Petition. While EPA believes that the updated risk assessment addresses the arguments raised in NRDC's petition regarding whether TCVP pet uses pose unacceptable risks, EPA declines to revisit the 2006 RED or to perform a new cumulative risk assessment for organophosphates at this time, and notes that registration review of TCVP is currently underway, pursuant to section 3(g) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), 7 U.S.C. § 136a(g), and 40 CFR Part 155.

The first section of this letter discusses the factual background relevant to NRDC's Petition. The second section of this letter summarizes the claims made in NRDC's Petition. The third section of this letter responds to those claims by discussing the assumptions, routes of exposure considered, and conclusions reached in EPA's updated non-occupational residential exposure assessment for all TCVP pet product uses, conducted in response to NRDC's Petition. The fourth section of this letter is the conclusion.

I. Background

TCVP is a member of the organophosphate (OP) class of pesticides. Like other OPs, TCVP's mode of action involves the inhibition of the enzyme acetylcholinesterase (AChE).

The RED for TCVP was initially completed in September 1995. An interim Tolerance Reassessment Eligibility Decision (TRED) for TCVP was completed in July 2002. A residential exposure assessment was originally completed in 1998 in support of the TRED, and concluded that residential risks to handler and post-application exposure were below the Agency's levels of concern. The residential assessment was refined in 2002. Both the TRED and 1998 assessment can be found in public docket number EPA-HQ-OPP-2002-0295 at www.regulations.gov. The Agency completed the OP cumulative risk assessment in July 2006, and as a result the TCVP TRED and RED were considered final at that time, and can be found in public docket number EPA-HQ-OPP-2006-0618. An update to the OP Cumulative risk assessment was completed in August 2006. There were no risks of concern identified in the residential assessment portion of the OP Cumulative, which considered exposure from the pet uses of TCVP. Additionally, the registration review docket for TCVP opened in 2008, and registration review is currently on-going. All registration review documents, as well as the RED, can be found in public docket number EPA-HQ-OPP-2008-0316.

On June 5, 2009, EPA announced receipt of NRDC's Petition to cancel all pet uses for TCVP in the Federal Register (74 FR 27035) and posted the petition in public docket number EPA-HQ-OPP-2009-0308 in regulations.gov for a 60-day public comment period, during which time interested stakeholders could review and comment on the Petition. The public comment period ended on August 4, 2009, during which time EPA received approximately 8,600 form letters as part of a mass campaign supporting NRDC's petitions to ban TCVP pet uses and propoxur pet collars.[1] In addition, the Agency also received a comment from The Humane Society of the United States (HSUS) that supported the petition and a comment from one TCVP registrant, Hartz Mountain Corporation, which opposed the petition. Substantive comments are addressed in a separate "Response to Comments" document, attached hereto as Appendix A. Regarding HSUS's comment about potential adverse reactions to TCVP of companion animals, the Agency is committed to studying this issue more closely to understand what additional measures, if any, may be appropriate to reduce the incidence of these unfortunate and avoidable events. While this comment does not pertain to the human health issues raised by NRDC's Petition, the Agency will conduct an in-depth review and analysis of pet incident data resulting from pet products that contain TCVP during the registration review process for TCVP.

Since the closing of the public comment period in 2009, the Agency has considered the Petition to cancel all TCVP pet products and the risks posed by TCVP pet products, especially to children. EPA has taken numerous steps to evaluate the concerns outlined in the Petition, including the completion of a new TCVP residential risk assessment which incorporates the most recent science policies and risk assessment methodologies to assess all available TCVP pet product uses. The results of this new assessment are discussed in section III of this letter, below.

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[1] On January 22, 2014, EPA published in the Federal Register, pursuant to section FIFRA § 6(f), a notice of receipt of registrant requests to voluntarily cancel all propoxur pet collar registrations. *See* 79 Fed. Reg. 3586 (Jan. 22, 2014). On March 26, 2014, EPA published in the Federal Register a notice announcing EPA's Order for the cancellation of all propoxur pet collar registrations. *See* 79 Fed. Reg. 16793 (Mar. 26, 2014). The effective date of the cancellations that are the subject of that Order is April 1, 2015. Accordingly, by letter dated October 9, 2014, EPA denied as moot NRDC's petition seeking cancellation of such registrations.

Along with the Petition, NRDC submitted an April, 2009 NRDC "Issue Paper" entitled "Poisons on Pets II: Toxic Chemicals in Flea and Tick Collars" (hereinafter "Poison on Pets II") for EPA's consideration of potential exposures from TCVP pet collars. However, this "Issue Paper" consisted only of the study overview and summarized findings along with a methodological appendix, and did not include the full study report including all the raw data. In a letter dated May 28, 2009, the Agency requested additional scientific information from NRDC so that EPA could fully analyze and independently verify the results of the study report, including all raw data and the protocol for the pet residue study. EPA also requested information on the ethical conduct of the study regarding the use of human subjects, as required by 40 CFR § 26.1303 under Subpart M – "Requirements for Submission of Information on the Ethical Conduct of Completed Human Research."

On June 25, 2009, NRDC submitted a response letter. Although NRDC's June 25, 2009 letter included a copy of the original protocol intended to support NRDC's argument that the studies underlying the "Poison on Pets II" report were not "human studies" under 40 CFR Part 26, the letter did not include either the scientific information to enable EPA to verify the results of the study report or the information on the ethical conduct of the studies required by 40 CFR § 26.1303. NRDC's letter stated:

> "... NRDC will await EPA's final determination that the study does not constitute research with human subjects and that the agency will include it as part of its assessment of our petitions. Once EPA makes that final determination, then we will provide the underlying data supporting our report." NRDC Letter, June 25, 2009, at 3.

In a letter dated August 7, 2009, EPA informed NRDC that the Agency (EPA's Office of Pesticide Programs, in consultation with EPA's Human Subjects Research Review Officer in the Office of the Science Advisor) still regarded the two studies described in the "Poison on Pets II" report as research with human subjects covered by EPA's rules in 40 CFR Part 26, "Protection of Human Subjects."

To date, NRDC has not submitted the necessary raw data to allow EPA to verify the "Poisons on Pets II" study findings. No other scientific information has been provided that would afford the Agency with a rationale to rely upon this study report for regulatory actions under FIFRA. Without the raw scientific data, this information could not be considered in EPA's evaluation of NRDC's Petition.

II. Petition Claims

NRDC's Petition argues that EPA did not assess the exposure from pet collar uses in the risk assessment underlying the RED, and that assumptions made pertaining to toddler exposures to TCVP were flawed in the OP cumulative risk assessment. NRDC argues that the decision to reregister TCVP pet uses was thus arbitrary and capricious and contrary to law, and that risks from pet uses of TCVP are unacceptable such that EPA should cancel such uses.

NRDC makes the following arguments in support of its position:

- **NRDC Argues that EPA Failed to Consider Pet Collar Exposures**: NRDC argues that despite finding that pet collar uses provided the highest exposure levels for adults,

EPA still chose not to conduct a risk assessment for pet collars, and that EPA ignored the possibility that the pet collar uses could expose infants and children to unsafe levels of TCVP.

- **NRDC Argues that EPA Used Faulty Exposure Assumptions**: NRDC argues that the EPA's organophosphate cumulative risk assessment for pet products significantly underestimated a toddler's exposure to residue on a pet from a flea collar. NRDC argues that the TCVP risk assessment assumed that toddlers were exposed for no more than one hour per day, but the EPA assumed a two hour per day exposure for toddlers in the dichlorvos (DDVP) case. NRDC further argues that EPA's underestimates include the use of hand-to-mouth activities at nine times per hour, while a published review of the scientific literature by EPA scientific experts indicated an average of 19.6 times per hour. NRDC further argues that the Agency failed to assess indirect hand-to-mouth activity, which is the exposure from toddlers who touch an object or food with pesticide-contaminated hands and then put that object or food into their mouths, while published studies show that there is noticeable indirect hand to mouth activity in infants and children.

- **NRDC Argues that Pet Collars Result in Unacceptably High Exposures**: NRDC argues that NRDC's report "Poison on Pets II" shows that residues of TCVP on the pets' fur are high enough to pose a significant risk to both children and adults who play with their pets.

III. EPA's Updated Risk Assessment for All TCVP Pet Uses

As noted above, in response to NRDC's Petition, EPA has conducted an updated non-occupational residential exposure assessment for all TCVP pet product uses. Based on that assessment, EPA does not find risks of concern resulting from pet uses of TCVP and therefore declines today to initiate cancellation action against such uses as requested in the petition. While EPA believes that the updated risk assessment addresses the arguments raised in NRDC's petition regarding whether TCVP pet uses pose unacceptable risks, EPA declines to revisit the 2006 RED or to perform a new cumulative risk assessment for organophosphates at this time, and notes that registration review of TCVP is currently underway, pursuant to FIFRA § 3(g) and 40 CFR Part 155.

In developing a response to this Petition, EPA considered, among other things, the information contained in the petition (to the extent it could without obtaining additional information from NRDC), new data relevant to the assessment of exposure from pet collars (*i.e.*, propoxur collar MRID 48589901), and updated residential exposure assessment methodologies, and the Agency completed a new residential exposure assessment for all TCVP pet product uses, entitled *Tetrachlorvinphos: Residential Exposure Assessment in Response to the Natural Resources Defense Council Petition to Cancel All Pet Uses for Tetrachlorvinphos*, dated November 5, 2014 (Attached hereto as Appendix B). This assessment concludes that all risks associated with TCVP pet products are below the Agency's level of concern (LOC) for all exposure scenarios. The key points of the assessment are outlined below, as part of the evaluation of NRDC's claims in its Petition.

EPA risk assessments rely on the most recent guidance and risk assessment methodologies available at the time they are completed. The human health risk assessments that NRDC's petition alleges failed to properly identify risks were originally completed in 1998 and 2006, and utilized exposure assumptions and methodologies based on Standard Operating Procedures (SOPs) for pet

product risk assessments in place at that time. The 2014 TCVP residential pet product assessment assessed residential handler and post-application risk from exposure to TCVP pet products using the Agency's 2012 SOPs for Residential Pesticide Exposure Assessment (available at http://www.epa.gov/opp00001/science/EPA-OPP-HED_Residential%20SOPS_Feb2012.pdf). Development of the 2012 SOPs included external peer review, including the Agency presenting a draft of the SOPs to the FIFIRA Scientific Advisory Panel (SAP) for comment in 2009. The updated residential exposure assessment also incorporates the following changes:

- the assumption of steady state exposures for TCVP exposure assessment;
- updated points of departure (PoDs) following re-evaluation of the TCVP toxicity database using the benchmark dose (BMD) techniques consistent with the methods currently used for other OPs;
- reduction of the total uncertainty factor (UF) for inhalation exposures from 100X to 30X due to use of the Agency's reference concentration (RfC) and human equivalent concentration (HEC) methodology;
- voluntary cancellation of TCVP trigger pump spray pet products (EPA Reg. Nos. 2596-122, 2596-123, and 2596-136);
- the re-evaluation of a previously submitted and reviewed pet residue transfer study for TCVP dust/powder and pump spray formulations; and
- the use of pet residue transfer study data specific to collar formulations.

The following is a summary of the analysis and conclusions found in the new 2014 TCVP residential risk assessment, entitled *Tetrachlorvinphos: Residential Exposure Assessment in Response to the Natural Resources Defense Council Petition to Cancel All Pet Uses for Tetrachlorvinphos.*

Toxicology and Uncertainty Factors

Like other OPs, the mode of action (MOA) for TCVP involves inhibition of the enzyme AChE via phosphorylation of the serine residue at the active site of the enzyme. This inhibition leads to accumulation of acetylcholine and ultimately to neurotoxicity in the central and/or peripheral nervous system. For TCVP, AChE inhibition is the most sensitive endpoint in the toxicology database in multiple species, durations, lifestages, and routes.

The toxicology database for TCVP is complete. TCVP has low acute toxicity by the oral, dermal, and inhalation routes of exposure. It is a slight dermal irritant, a moderate eye irritant, and a dermal sensitizer. TCVP is classified as a possible human carcinogen (Group C) based on statistically significant increases in combined hepatocellular adenoma/carcinomas in mice, and suggestive evidence of thyroid c-cell adenomas and adrenal pheochromocytomas in rats. The mutagenicity database for TCVP suggests that this chemical was not mutagenic in both the gene mutation assay and primary rat hepatocyte unscheduled DNA synthesis assay. However, this chemical was positive for inducing chromosomal aberrations in Chinese hamster ovary cells in the absence of metabolic activation, but was negative in the presence of metabolic activation. Immunotoxicity was not observed at dose levels that exceed the limit dose.

As with other OPs, TCVP exhibits a phenomenon known as steady state AChE inhibition. After repeated dosing at the same dose level, the degree of inhibition comes into equilibrium with the production of new, uninhibited enzyme. At this point, the amount of AChE inhibition at a given dose remains consistent across duration. In general, OPs reach steady state

within 2-3 weeks, but this can vary among OPs. TCVP shows a shallow dose-response curve for cholinesterase inhibition; in other words, large increases in administered dose result in only small changes in AChE inhibition.

Based on the robust dataset from the OP cumulative risk assessment across the OPs, exposure assessments of 21 days and longer will be conducted for all routes of exposure; *i.e.,* oral, dermal, and inhalation, for all single chemical OP assessments. Given this, the 21-day and longer exposure assessment is scientifically supportable and also provides consistency with the OP cumulative risk assessment and across the OP registration review risk assessments.

The Food Quality Protection Act (FQPA) children's safety factor (SF) was reduced to 1X since there is no evidence of sensitivity of the young animal compared to the adult and there are no data gaps. A total uncertainty factor (UF) of 100X is appropriate for dermal and incidental oral routes of exposure (10X for interspecies extrapolation, 10X for intraspecies variation, and 1X FQPA SF). For the inhalation route of exposure, a total SF of 30X (3X for interspecies extrapolation, 10X for intraspecies variation, and 1X FQPA SF) is appropriate. The interspecies extrapolation is reduced from 10X to 3X because the reference concentration (RfC) methodology for inhalation is used to determine a human equivalent concentration (HEC) and takes into consideration the pharmacokinetic differences between animals and humans.

Residential Handler Exposures

Residential exposures are anticipated from the use of TCVP pet products. Residential TCVP handler exposures are anticipated to be short- (1 to 30 days) to intermediate-term (1 to 6 months) in duration. However, because of the steady state AChE inhibition exhibited by the OPs, steady state exposures (21 days and longer) were assessed and presented for residential exposures to TCVP pet products.

Residential handler exposures to TCVP pet products may occur via the dermal or inhalation routes while the product is placed on a cat or dog. A steady state residential handler exposure assessment (combined dermal and inhalation) was performed for homeowners applying TCVP products to cats and dogs. A residential handler cancer assessment was conducted due to TCVP being classified as a Group C possible human carcinogen by the Agency with a linear low-dose approach for quantification of risk using the oral slope factor (Q1*) of 1.83×10^{-3} $(mg/kg/day)^{-1}$.

A series of assumptions and exposure factors served as the basis for completing the residential handler risk assessment, which are detailed below.

Per the SOPs, it is assumed that residential handlers of pet treatment products will treat two animals per application. For TCVP dust and powder products, all products identify a specific amount to use per animal weight that allows for determination of the maximum application rate. For TCVP pump sprays, all registered products direct the user to apply a specific number of "strokes" per animal size. In order to determine the amount of active ingredient (a.i.) applied per treatment as specified by number of strokes, EPA requested additional information from a product registrant, Hartz Mountain Corporation, which holds most of the TCVP pet product registrations. Hartz provided information regarding the total volume of product released per stroke for pump and trigger spray products; 0.19 and 0.93 grams, respectively. Only trigger spray products are available for dogs; however, both pump and trigger spray products are available for cats. Additionally, Hartz Mountain Corporation submitted an application for amendment to the product

label of EPA Reg. No. 2596-140, which was approved by the Agency in March 2014, to recommend a number of strokes per animal size. The specific number of strokers per animal size is located in Table 4.0 in the 2014 residential assessment. Previously, a number of strokes per cat/dog was not recommended.

For TCVP collars, the applicator is directed to cut off and dispose of any excess length once the product is fit and buckled into place. As described in the SOPs, because the exact length cannot be determined, the corresponding a.i. loss cannot be quantified and, therefore, exposure is conservatively assessed assuming the full collar length.

A series of assumptions and exposure factors served as the basis for completing the residential handler risk assessment. Each assumption and factor is detailed in the SOPs.

Unit Exposures and Area Treated or Amount Handled: Chemical-specific unit exposure data were provided in support of the residential handler risk assessment for the dust/powder formulations only (MRID 45519601). The study, "Determination of Dermal and Inhalation Exposures to Tetrachlorovinphos (TCVP) During the Application of an Insecticide Powder to a Dog," was previously reviewed by the Agency in January 2002 and determined to be acceptable, and the data was reflected in the TRED for TCVP in 2002. These exposure data were used as a surrogate to estimate handler exposures from the TCVP dust/powder products. The study resulted in average unit exposures for the dermal and inhalation routes of exposure of 1,700 mg/lb a.i. and 3.1 mg/lb a.i., respectively.

In the absence of exposure data for residential handling of pet collars and pump/trigger sprays, the Agency used exposure values from the 2012 Residential SOPs: Treated Pets as a surrogate to estimate handler exposures. Surrogate exposure data for a groomer trigger pump spray application to dogs was used to estimate handler exposures from TCVP pump spray products. No exposure data are available for assessment of handler exposures from the application of collars. In the absence of formulation-specific data, exposure data for spot-on applications was used to estimate handler exposures from the TCVP collar products.

Exposure Duration: Residential handler exposure is expected to be short-term in duration. Intermediate- and long-term exposures are not likely because of the intermittent nature of applications by homeowners. Steady state exposures (21 days and longer) were assessed and presented for residential handler exposures to TCVP pet products because of the steady state AChE inhibition exhibited by the OPs.

Days per Year of Exposure: For the purpose of assessing residential handler cancer exposure/risk from TCVP product application, EPA has assumed four days per year for collars, and 6 days per year for dusts/powders and pump sprays. The collar is based on a worst-case assumption of a single application every three months. Collar re-treatment intervals range from three to seven months. EPA assumed a bi-monthly re-treatment interval for dusts/powders and pump sprays.

Years per Lifetime of Exposure and Lifetime Expectancy: It is assumed that residential handler exposure would occur for 50 years out of a 78 year lifespan. This factor is routinely used as a conservative estimate of the number of years an individual could continually use a single pesticide product. Life expectancy values are from the Exposure Factors Handbook 2011 Edition Table 18-1 (U.S. EPA, 2011). The table shows that the overall life expectancy is 78 years based on life expectancy data from 2007. In 2007, the average life expectancy for males was 75 years and 80 years

for females. Based on the available data, the recommended value for use in cancer risk assessments is 78 years.

Residential Handler Risk Estimates and Conclusions

EPA concluded that residential handler (adults) combined steady state (dermal and inhalation) exposures are not of concern to the Agency (*i.e.*, all aggregate risk indexes (ARIs) are greater than 1) from application of any registered TCVP pet products. A complete listing of all ARIs can be found in Table 5.1.1 in the 2014 residential assessment. The ARI approach was required to combine the dermal and inhalation routes of exposure because of the different LOCs. LOCs recommended for the dermal and inhalation routes of exposure are margins of exposure (MOEs) of 100 and 30, respectively. ARIs of less than 1 indicate risks of concern. The ARI approach normalizes MOEs from different routes to an LOC of 1 to facilitate aggregation of risks, as described in the Agency's *General Principles for Performing Aggregate Exposure and Risk Assessments*.[2]

Estimated residential handler cancer risk estimates range from 10^{-9} to 10^{-7}, which are below the Agency's LOC. A complete listing of all residential handler cancer exposure and risk estimates can be found in Table 5.1.2 in the 2014 residential assessment.

Residential Post-application Exposure

EPA identified that there is the potential for post-application exposure for individuals exposed as a result of contacting a cat or dog previously treated with TCVP pet products. The quantitative exposure risk assessment for residential post-application exposures is based on the following scenarios:

1) Post-application dermal (adults and children 1 to < 2 years old) exposure from contacting cats and dogs treated with TCVP; and
2) Post-application incidental oral exposure (children 1 to < 2 years olds only) from contacting cats and dogs treated with TCVP.

Residential post-application inhalation exposure is expected to be negligible from TCVP pet products and, thus, a quantitative assessment was not performed. Per the Residential SOPs, the combination of low vapor pressure (2.6×10^{-7} mmHg at 25°C) and the small amounts of pesticide applied to pets is expected to result in negligible levels of chemical in the air, and therefore negligible inhalation exposures.

A series of assumptions and exposure factors served as the basis for completing the residential post-application risk assessment. Each assumption and factor is detailed in the SOPs.

Exposure Data: Surrogate and chemical-specific residue transfer studies were used for assessment of post-application exposures from registered TCVP pet products. These exposure data include the following residue transfer studies: propoxur collar (MRID 48589901); and TCVP powder and pump spray (MRID 45485501).

[2] http://www.epa.gov/opp00001/trac/science/aggregate.pdf

EPA previously conducted a data evaluation record (DER) of the TCVP exposure study for aerosols, powders, and pump sprays[3] in 2001. In support of the Agency's response to the NRDC petition, the study has been re-evaluated based on current standards of conduct for pet residue transfer studies[4]. The re-evaluation of the TCVP residue transfer study resulted in a number of changes from the 2001 DER. Table 5.2.1 from the 2014 residential assessment below presents a comparison of the methods used to evaluate the study data.

Comparison of 2001 and Current TCVP Pet Residue Transfer Study Reviews	
2001 Review	Current Review
Handwipe residue data were corrected for average field fortification recoveries <90%.	Handwipe residue data were corrected for average field fortification recoveries <120%.
TCVP residues on hands in µg/cm² were calculated using the surface area of the stroking area (defined as length of dog x length of study participant's hand).	TCVP residues are calculated in µg/cm² using the surface area of the entire dog, based on the weight of the test animal.
The percent of applied TCVP dislodged by the hand following treatment was calculated based on the amount of TCVP residue on the stroking area, which was determined from extrapolating residues detected in fur samples from a shaved area to the area of the stroking area.	The percent of applied TCVP transferred to the hand was calculated based on the total amount of active ingredient applied to the dog (calculated as the amount removed from container in grams x actual percent active ingredient in test product).
Regression analyses were conducted using the residue data in µg/cm².	The revised regression analyses were conducted using the percent of applied dose transferred to the hand.

It should be noted that the TCVP powder and pump spray post-application exposure study was not conducted in a manner reflective of current standards that require a defined stroking procedure and greater number of petting simulations. That is, the pet is to be stroked in a single motion with the grain of the fur starting with both sides (along the ribcage) of the cat or dog and followed by the same motion along the back (dorsally) from the base of the neck to the tail. The two sides and back, in this order, account for one petting simulation. A total of 20 petting simulations (or 60 stroking motions) are currently required. In the TCVP post-application exposure study, the dogs were stroked on only one side of the treated dog's back from head to rump five times. However, the study was reflective of current policy regarding pet residue transfer studies at the time that it was conducted. In order to account for the differences between the TCVP post-application exposure study and the currently recommended standard, the Agency used the maximum observed percent residue transfer on the day of product application (Day 0) for both formulations for exposure and risk quantification. Typically, the Agency assesses post-application risk with use of the mean percent residue transfer measured on Day 0; the use of the maximum value results in a more health protective risk assessment. Even though the post-application exposure study methods have evolved, the TCVP study employed a rigorous collection method and is not anticipated to underestimate exposure.

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[3] S. Hanley. Re-evaluation of *Determination of the Dislodgeability of Tetrachlorvinphos (TCVP) from the Fur of Dogs Following the Application of an Insecticide Powder, Pump Spray or Aerosol.* 3/25/02. D277543.
[4] W. Britton. Tetrachlorvinphos: Reevaluation of "HED's Review of *Determination of the Dislodgeability of Tetrachlorvinphos (TCVP) from the Fur of Dogs Following the Application of an Insecticide Powder, Pump Spray or Aerosol*; MRID 45485501. 5/16/14. D420285.

Exposure Duration: Residential post-application exposure is expected to be short- and intermediate-term for dust/powders and pump/trigger sprays. For pet collars, post-application exposures is expected to be long-term (greater than 6 months) due to the potential for extended usage in more temperate parts of the country, and the longer active lifetime of pet collar products. Again, because of the steady state AChE inhibition exhibited by the OPs, steady state exposures (21 days and longer) were assessed and presented for residential post-application exposures to TCVP pet products.

Hand-to-Mouth Event Frequency: The 2012 Residential SOPs include a frequency estimate of 20 as the modeled number of hand-to-mouth events per hour for children 1-2 years old. There are currently no data available that specifically address the number of hand-to-mouth events that occur relative to the amount of time that a child spends with a pet. As a result, the estimate for frequency of hand-to-mouth events in indoor environments is based on the Xue et al. (2007)[5] meta-analysis of child hand mouthing frequency. The indoor data were selected, even though child exposure to treated pets can occur either indoors or outdoors, because the indoor data result in a greater frequency of contacts and, therefore, a more health protective risk assessment. Please see Table A.2 in Appendix A of the 2014 residential assessment for more information on hand-to-mouth exposure inputs.

Years Per Lifetime of Exposure and Lifetime Expectancy: It is assumed that residential post-application exposure would occur for 50 years out of a 78 year lifespan. This factor is routinely used as a conservative estimate of the number of years an individual could continually use a single pesticide product. Life expectancy values are from the Exposure Factors Handbook 2011 Edition Table 18-1 (U.S. EPA, 2011). The table shows that the overall life expectancy is 78 years based on life expectancy data from 2007. In 2007, the average life expectancy for males was 75 years and 80 years for females. Based on the available data, the recommended value for use in cancer risk assessments is 78 years.

Pet Contact: For the purpose of determining exposure to treated pets, the 2012 Residential SOPs make use of transfer coefficients (TCs). TC is an exposure rate for a selected activity which involves contact with a source, such as children playing with treated pets or on treated turf. The TC concept is a long-standing established approach used to estimate residential, as well as occupational exposures, and is the basis for the Agency's post-application exposure guidelines[6]. A TC is derived by taking the ratio of study volunteer dermal exposure per unit time (mg/hr), and the concurrent measure of residue transfer. Ideally, dermal exposure is based on activities representative of the use pattern and residue transfer is determined by use of an established method specific to the use pattern. For pet exposures, TCs can be defined as animal surface area contact per unit time (cm^2/hr).

Currently, there is no exposure study available using typical adult and child activities with pets and a concurrent transferable residue (TR) measure. In the absence of direct exposure data for residential activities with pets, the Agency concluded that studies conducted to monitor pet grooming activities are likely to result in a highly protective estimate of pet contact relative to

[5] Xue, J., Zartarian, V., Moya, J., Freeman, N., Beamer, P., Black, K., Tulve, N., Shalat, S. (2007), A Meta-Analysis of Children's Hand-to-Mouth Frequency Data for Estimating Nondietary Ingestion Exposure. Risk Analysis, 27(2):411-420.

[6] http://www.ecfr.gov/cgi-bin/text-idx?SID=6bfd453976f1be8d5b20dfbf6bc19b9d0&node=40:25.0.1.1.9.9&rgn=div6

contact associated with petting, hugging, or sleeping with a pesticide-treated pet. These data were gathered while human volunteers applied dust/powders and shampoo products to various dogs of differing sizes and fur lengths. Since these individuals extensively handled the dogs, it is expected that their resulting exposures are higher than would be reasonably anticipated from routine contact with treated pets. The volunteers in the shampoo study, who were professional groomers, shampooed 8 dogs for 5 minutes each, rinsed, and lifted them to counters for drying and combing resulting in very high exposures. In the dust study, volunteers applied dust via shaker can to 8 dogs each and then rubbed the dusts into the dogs' coats. The applicator studies were not conducted in a manner which measured TR, or active ingredient pet surface area. Therefore, the residue available on the animal for transfer was predicted by multiplying the arithmetic mean fraction of application rate from the analysis of all liquid formulated product data sets presented in the 2012 Residential SOPs, 0.96%. This approach has the effect of increasing TC estimates, thus resulting in TC values which are more protective of human health. Furthermore, the selection of the mean value, in lieu of the screening level fraction application rate (F_{AR}) value, 2%, further increases the TC estimates with use of the dust and shampoo studies.

Exposure Time: The exposure time (ET) assumption used to assess residential post-application exposure to TCVP pet products is derived from a study which sought to evaluate the times that individuals spend performing different activities around the home. Based upon the 2012 Residential SOPs, the point estimates recommended for adult and child ET with pets are 0.77 and 1 hours, respectively. In the study, animal care is defined as "care of household pets including activities with pets, playing with the dog, walking the dog and caring for pets of relatives, and friends." The data identified the time spent with an animal while performing household activities as recorded in 24 hour diaries by study volunteers. While the activities defined do not necessarily represent the time volunteers were actively engaged in constant contact with the animal as is implicit in the post-application dermal and incidental oral algorithms, the data are the most accurate representation of time spent with pets available and, therefore, it is assumed that contact is continual throughout the timed activity. The Agency assumes the ET value reflects a reasonable high end estimate of time spent in contact with a dog treated with TCVP pet products.

When use of the study data are coupled with high end assumptions of pet contact, the result is an exposure assessment that inherently implies vigorous, continual contact for the entire duration of contact. While it is possible that an adult or child may be in close contact with a pet intermittently throughout the day, they would not be actively engaged in the highly vigorous contact implied by use of the TCs based on the applicator exposure data for the full exposure duration assumed. Further, it is possible that adults or children may be exposed from sleeping with a treated pet; however, they are not actively engaged in a high level of contact, or the repeated mouthing behaviors exhibited by children during waking hours, which are inherently assumed in the assessment conducted.

Residential Post-application Risk Estimates and Conclusions

Residential post-application steady state adult dermal (only) exposure and children 1 to 2 years old combined (dermal and incidental oral exposures) are not of concern to the Agency (*i.e,* all MOEs are greater than 100) for all TCVP pet products assessed. The combined MOE approach was used because the dermal and incidental oral routes of exposure have the same LOC. MOEs under 100 indicate risks of concern. The residential post-application MOEs range from 270 to 43,000. A complete listing of all MOEs can be found in table 5.2.2 in the residential assessment. Estimated residential handler cancer risk estimates range from 10^{-9} to 10^{-7}, and residential post-

application cancer risk estimates range from 10^{-8} to 10^{-6}, which are below the Agency's LOC. A complete listing of all residential post-application cancer exposure and risk estimates can be found in Table 5.2.3 in the 2014 residential assessment.

It should also be noted that the evaluation of the potential residential post-application health risks from exposures to cats and dogs treated with TCVP pet products is conservative. The risk estimates calculated are based upon protective assumptions of TCVP hazard, product application rates, durations of exposure, and contact with the treated animal, and they make use of the best available post-application exposure data.

For a more detailed explanation of residential exposure from the use of pet products containing TCVP and the Agency's conclusions, please refer to the 2014 TCVP residential risk assessment, entitled *Tetrachlorvinphos: Residential Exposure Assessment in Response to the Natural Resources Defense Council Petition to Cancel All Pet Uses for Tetrachlorvinphos.*

IV. Conclusion

The 2014 residential assessment discussed above uses appropriate, validated methodologies to calculate potential exposure to TCVP pet products and shows that all identified risks associated with TCVP pet uses (including pet collars) result in risks that are below the Agency's level of concern. Again, while EPA believes that the updated risk assessment addresses the arguments raised in NRDC's petition regarding whether TCVP pet uses pose unacceptable risks, EPA declines to revisit the 2006 RED or to perform a new cumulative risk assessment for organophosphates at this time, and notes that registration review of TCVP is currently underway, pursuant to FIFRA § 3(g) and 40 CFR Part 155. Therefore, NRDC's petition to cancel all pet uses for TCVP due to alleged risks of concern is hereby denied.

Please contact Kelly Ballard at (703) 305-8126 or ballard.kelly@epa.gov, if you have any questions or concerns regarding this response.

Sincerely,

By [signature], Acting

Jack E. Housenger, Director
Office of Pesticide Programs

Exhibit H

Case No. _____

UNITED STATES COURT OF APPEALS
FOR THE NINTH CIRCUIT

NATURAL RESOURCES DEFENSE COUNCIL, INC.,

Petitioner,

v.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY,

Respondent.

PETITION FOR REVIEW
Of An Order Of The U.S. Environmental Protection Agency

Mae Wu
NATURAL RESOURCES DEFENSE COUNCIL
1152 15th Street, NW, Suite 300
Washington, D.C. 20005
Telephone: (202) 289-6868
mwu@nrdc.org

Susannah Landes Weaver
Kelsi Brown Corkran
ORRICK, HERRINGTON & SUTCLIFFE
1152 15th St. NW
Washington, DC 20005
Telephone: (202) 339-8400
Facsimile: (202) 339-8500
sweaver@orrick.com

Counsel for Petitioner

Dated: January 5, 2015

PETITION FOR REVIEW

Pursuant to Rule 15 of the Federal Rules of Appellate Procedure and section 16(b) of the Federal Insecticide, Fungicide, and Rodenticide Act, 7 U.S.C. § 136n(b), Natural Resources Defense Council ("NRDC") hereby petitions this Court to review and set aside the final order of the U.S. Environmental Protection Agency ("EPA") denying NRDC's request to cancel all pet uses of the pesticide tetrachlorvinphos (Chemical Abstract Number 22248-79-9). The challenged final order was announced in a regulatory decision document that was entered on EPA docket EPA-HQ-OPP-2009-0308 with a date of signature of November 6, 2014. The order became final on November 20, 2014, at 1:00 p.m. eastern time, pursuant to 40 C.F.R. § 23.6. A copy of this final regulatory decision document is attached as Exhibit A to this petition.

Dated: January 5, 2015

Respectfully submitted,

/s/ Susannah Landes Weaver
ORRICK, HERRINGTON & SUTCLIFFE
1152 15th Street, NW
Washington, D.C. 20005
Telephone: (202) 339-8500
Facsimile: (202) 339-8400
sweaver @orrick.com

Exhibit I

ORAL ARGUMENT NOT YET SCHEDULED

No. 15-70025

UNITED STATES COURT OF APPEALS
FOR THE NINTH CIRCUIT

NATURAL RESOURCES DEFENSE COUNCIL, INC.,

Petitioner,

v.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY,

Respondent.

RESPONDENT'S OPPOSED MOTION FOR VOLUNTARY REMAND

Pursuant to Federal Rule of Appellate Procedure 27, Respondent United States Environmental Protection Agency ("EPA" or "Agency") hereby moves for a voluntary remand of EPA's November 6, 2014 response ("the Response") to Petitioner Natural Resources Defense Council's ("NRDC") April 23, 2009 Petition Requesting Cancellation of All Pet Uses of Tetrachlorvinphos. Counsel for NRDC have represented that NRDC opposes this motion.

This case concerns EPA's administration of the Federal Insecticide, Fungicide, and Rodenticide Act ("FIFRA") and EPA's response to an administrative petition requesting that the Agency cancel all registered pet uses of

a pesticide, tetrachlorvinphos. In its Response, EPA concluded that cancelling registration of tetrachlorvinphos for pet uses was not warranted based, in large part, on a risk assessment that EPA conducted in response to NRDC's 2009 petition.[1] However, as part of its independent statutory obligation to periodically evaluate pesticides to ensure that they continue to meet registration standards, EPA is in the process of preparing a new risk assessment for tetrachlorvinphos. EPA anticipates that this new risk assessment—a draft of which will be released by the end of this year—will differ in a number of material ways from the earlier assessment relied upon by EPA in responding to NRDC's petition. EPA intends to review its prior response in light of the new risk assessment. Accordingly, remand would best serve the interests of judicial economy. EPA's reevaluation of its Response in light of the new risk assessment could moot or significantly narrow the issues raised by NRDC in this litigation.

BACKGROUND

FIFRA, 7 U.S.C. §§ 136-136y, requires EPA approval of pesticides prior to their distribution or sale and establishes a registration regime for regulating the use of pesticides. 7 U.S.C. § 136a(a). EPA must approve an application for pesticide registration if, among other things, the pesticide will not cause unreasonable

[1] The Response is attached to NRDC's Petition for Review [Dkt 1-2].

adverse effects on the environment. *Id.* § 136a(c)(5). Section 3(g) of FIFRA, 7 U.S.C. § 136a(g), requires EPA to periodically reevaluate pesticides through a process known as "registration review" in order to ensure that they continue to meet the standards for registration.

Tetrachlorvinphos is a member of the organophosphate class of pesticides that act by inhibiting the enzyme acetylcholinesterase. Tetrachlorvinphos was first registered in 1966 and is primarily used on livestock and pets to control insects like fleas. In 2006, EPA reregistered tetrachlorvinphos after conducting a residential risk assessment for exposures to tetrachlorvinphos and a cumulative risk assessment for exposures to all organophosphates.[2] *See* Response at 2.

On April 23, 2009, NRDC petitioned EPA to cancel all pet uses for tetrachlorvinphos, arguing, among other things, that EPA's tetrachlorvinphos risk assessment failed to take into account exposures from pet collars. *See* Ptr.'s Br., ER58-ER63 [Dkt. 16-3]. In response to NRDC's 2009 petition, EPA conducted a residential risk assessment of the pet uses of tetrachlorvinphos (including pet

[2] The process EPA uses for evaluating the potential for health and ecological effects of a pesticide is called risk assessment, which is part of a risk management process. In registration review, that risk assessment includes an ecological risk assessment, a human health risk assessment, and, when appropriate, a cumulative risk assessment (evaluating the risk of a common toxic effect associated with concurrent exposure by all relevant pathways and routes of exposure to a group of chemicals that share a common mechanism of toxicity).

collars) using the most recent science policies and methodologies available at the time. As explained in the Agency's Response, EPA concluded in its risk assessment that the potential risks of exposure to tetrachlorvinphos from pet products were below the Agency's level of concern. *See* Response at 4-12. EPA relied on this risk assessment, among other things, when the Agency denied NRDC's request to cancel all pet uses of tetrachlorvinphos on November 6, 2014.

As part of its ongoing registration review for tetrachlorvinphos and other organophosphate pesticides, EPA's Office of Pesticide Programs is conducting a new risk assessment for all uses (not just pet uses) of tetrachlorvinphos. Declaration of Richard Keigwin, Jr., ¶ 4, attached as Exhibit 1. Although this risk assessment is being conducted as part of an ongoing registration review and independently from this litigation, EPA will be considering many of the scientific issues raised in this litigation in preparing the risk assessment. *Id.* ¶ 6. This new risk assessment is likely to differ in a number of ways from the earlier risk assessment relied upon by EPA in responding to NRDC's petition. Most notably, it is EPA's current intention to retain the presumptive tenfold margin of safety identified in section 408(b)(2)(C) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 346a(b)(2)(C), in the new risk assessment, *see* Keigwin Decl. ¶ 5; this

tenfold safety factor was not retained in the earlier assessment.[3] The issue of whether the tenfold safety factor should have been retained in the earlier assessment is an important issue raised by NRDC in this case. *See* Ptr.'s Br. at 37-46.

EPA expects to issue a draft of the new risk assessment by the end of 2015, i.e., in the next three months. Keigwin Decl. ¶ 4. EPA will publish the draft risk assessment in the Federal Register and open a 60-day public comment period. *Id.* ¶¶ 7-8. Once EPA has considered any public comments submitted, the Agency will finalize the risk assessment. *Id.* ¶ 10. EPA intends to then issue a revised response to NRDC's 2009 petition, considering the new final risk assessment for tetrachlorvinphos, within 90 days of finalizing that new assessment. *Id.*

EPA approached NRDC in mid-August 2015 to discuss EPA's intention to review its Response to NRDC's petition in light of the registration review risk assessment. EPA advised NRDC of its intent to retain the presumptive tenfold safety factor in the development of the registration review risk assessment. EPA further notified NRDC that, when preparing the new registration review risk assessment, EPA intends to consider all of the other major concerns raised by

[3] The Food Quality Protection Act, which amended FIFRA in 1996, requires EPA to apply "an additional tenfold margin of safety" to protect against harm to infants and children, unless EPA has "reliable data" that a different margin of safety "will be safe for infants and children." 21 U.S.C. § 346a(b)(2)(C).

NRDC in its August 5, 2015 opening brief [Dkt. 16] in the context of the evolving science on organophosphates. On September 18, 2015, following lengthy discussions between the parties, NRDC counsel represented that they would oppose this motion for remand.[4]

ARGUMENT

"A reviewing court has inherent power to remand a matter to the administrative agency." *Loma Linda Univ. v. Schweiker*, 705 F.2d 1123, 1127 (9th Cir. 1983) (citation omitted). "[I]t is generally accepted that in the absence of a specific statutory limitation, an administrative agency has the inherent authority to reconsider its decisions." *Macktal v. Chao*, 286 F.3d 822, 825-26 (5th Cir. 2002) (citation omitted); *Trujillo v. Gen. Elec. Co.*, 621 F.2d 1084, 1086 (10th Cir. 1980) (noting that "the power to decide in the first instance carries with it the power to reconsider") (citation omitted). This authority includes the right to seek voluntary remand of a challenged agency decision, without confessing error. *SKF USA Inc. v. United States*, 254 F.3d 1022, 1029 (Fed. Cir. 2001).

While the reviewing court has discretion on whether to remand, voluntary remand is appropriate where the request is reasonable and timely. *Macktal*, 286

[4] EPA's response brief is currently due October 5, 2015. Pursuant to Circuit Rule 27-11(a)(3), the filing of this motion stays the briefing schedule pending the Court's disposition of the motion.

F.3d at 826. "Administrative reconsideration is a more expeditious and efficient means of achieving adjustment of agency policy than is resort to the federal courts." *B.J. Alan Co. v. ICC*, 897 F.2d 561, 562 n.1 (D.C. Cir. 1990) (*quoting Commonwealth of Pa. v. ICC*, 590 F.2d 1187, 1194 (D.C. Cir. 1978)). "Generally, courts only refuse voluntarily requested remand when the agency's request is frivolous or made in bad faith." *Cal. Cmtys. Against Toxics v. EPA*, 688 F.3d 989, 992 (9th Cir. 2012) (citation omitted).

Here, EPA is conducting a new assessment of the potential risks of exposure to tetrachlorvinphos with the benefit of scientific policies and methodologies that have evolved since the Agency's 2014 Response. As part of that new assessment, EPA currently intends to retain the children's tenfold safety factor, and also intends to address the other major concerns raised by NRDC in this proceeding. Based on the new assessment, EPA further intends to reevaluate NRDC's petition and revise its Response as appropriate.[5]

Remand of EPA's Response will serve the interests of judicial economy by possibly mooting or significantly narrowing the issues that NRDC has raised in

[5] Although EPA intends to reevaluate NRDC's petition based on new scientific evidence, EPA does not admit that it erred in denying NRDC's petition based on the record before it at the time of the decision.

this litigation.[6] Additionally, remand will serve to improve the record as EPA's renewed response to the arguments raised by NRDC in its petition for cancellation of the pet uses of tetrachlorvinphos will be informed by the conclusions reached in the new risk assessment.

Granting this motion additionally promotes efficiency because remand is the ultimate outcome that NRDC seeks in this litigation. *See* Ptr.'s Br. at 71 ("[T]he case should be remanded to EPA to cancel the registrations for TCVP pet products or adequately explain why refusing to do so does not result in unreasonable adverse effects to children's health."). Thus, even if NRDC prevailed in its challenge to EPA's 2014 action—an action that is being reconsidered by EPA[7]—there would still need to be further administrative proceedings regarding whether any cancellation of the registrations is warranted, and it would be EPA's responsibility to set a reasonable timetable for responding to NRDC's petition on

[6] EPA was not in a position to seek remand of its Response until after NRDC filed its opening brief on August 5, 2015, because registration review proceeds on an independent timeline. Nonetheless, EPA is committed to considering the major arguments raised in NRDC's brief, which will maximize the effectiveness of remand and ensure that NRDC's efforts preparing its brief were not wasted.

[7] EPA does not confess any error based on the record before EPA at the time of the 2014 action.

remand.[8] EPA is simply proposing to move forward with remand now, rather than wasting judicial and governmental resources litigating over an earlier decision that EPA is already in the process of administratively reconsidering. Denying EPA's motion for voluntary remand would just compel EPA to devote limited resources to this litigation, as opposed to completing the ongoing scientific review process.

EPA intends to conclude reconsideration of NRDC's petition within a reasonable period of time. Specifically, EPA intends to issue the new draft risk assessment by the end of 2015, publish the draft risk assessment for the 60-day comment period, and issue a revised response to NRDC's petition within 90 days after finalizing the risk assessment. While EPA cannot determine how long it would take to issue a final risk assessment until it sees the volume and complexity of public comments that may be submitted in response to the draft risk assessment, EPA will be able to provide an estimate of how much time it would take to complete the final assessment within 45 days of the close of the comment period. Keigwin Decl. ¶ 10.

In short, remand would promote judicial and governmental economy by possibly mooting or significantly narrowing the issues that NRDC has raised in

[8] Mandamus is the appropriate remedy for any unreasonable agency delay. *See, e.g., NRDC v. EPA*, 489 F.3d 1364, 1375 (D.C. Cir. 2007). *See also Int'l Union, United Mine Workers of Am. v. Dep't of Labor*, 554 F.3d 150, 155 (D.C. Cir. 2009) (declining to impose schedule on remand).

this litigation, and by facilitating the Agency's ability to devote its limited resources to completing the scientific review process rather than to this litigation.

CONCLUSION

For the foregoing reasons, EPA respectfully requests that the Court remand the Response to the Agency for further consideration.

Dated: September 25, 2015

Respectfully submitted,

JOHN C. CRUDEN
Assistant Attorney General
Environment & Natural Resources Division

s/ *Erica M. Zilioli*
ERICA M. ZILIOLI
U.S. Department of Justice
Environmental Defense Section
P.O. Box 7611
Washington, DC 20044
Telephone: (202) 514-6390
Facsimile: (202) 514-8865
Erica.Zilioli@usdoj.gov

Of Counsel:

BENJAMIN WAKEFIELD
Office of General Counsel
U.S. Environmental Protection Agency
William Jefferson Clinton Building North
1200 Pennsylvania Avenue, N.W.
Washington, DC 20460

Exhibit J

No. 15-70025

UNITED STATES COURT OF APPEALS
FOR THE NINTH CIRCUIT

NATURAL RESOURCES DEFENSE COUNCIL, INC.,

Petitioner,

v.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY,

Respondent.

DECLARATION OF RICHARD P. KEIGWIN, JR. IN SUPPORT OF RESPONDENT'S MOTION FOR VOLUNTARY REMAND

I, Richard P. Keigwin, Jr., state the following:

1. I declare that the following statements are true and correct to the best of my knowledge and belief and are based upon my personal knowledge and/or my review of information contained in the records of the United States Environmental Protection Agency ("EPA" or the "Agency") or supplied by current employees.

2. I am the Director of the Pesticide Re-evaluation Division ("PRD") in EPA's Office of Pesticide Programs ("OPP"). I have worked for EPA for over 25 years. Since August 1993, I have served in various positions within OPP, including Acting Director of the Biological and Economic Assessment Division ("BEAD") from March 2005 to February 2006. I was the Director of BEAD from February 2006 to January 2009. I have been the Director of PRD, formerly the Special Review and Reregistration Division, since January 2009.

3. PRD is the division assigned with the responsibility to develop EPA's regulatory position regarding the re-evaluation of conventional pesticides that are currently registered under the Federal Insecticide, Fungicide, and Rodenticide Act ("FIFRA"). Part of PRD's responsibility includes overseeing the periodic "registration review" of conventional pesticides as required by section 3(g) of FIFRA, 7 U.S.C. § 136a(g).

4. The pesticide tetrachlorviphos ("TCVP") is currently undergoing registration review, per FIFRA § 3(g), 7 U.S.C. § 136a(g). In the context of that

registration review, EPA is conducting a human health risk assessment of TCVP, a draft of which EPA anticipates will be published for public comment by the end of calendar year 2015.

5. It is EPA's current belief that the draft risk assessment to be published in the context of the TCVP registration review will retain the "additional tenfold margin of safety … for infants and children" (the "10X safety factor") described by section 408(b)(2)(C) of the Federal Food, Drug, and Cosmetic Act ("FFDCA"), 21 U.S.C. § 346a(b)(2)(C).

6. It is EPA's current intention and belief that the draft risk assessment to be published in the context of the TCVP registration review will address each of the major points raised by the Natural Resources Defense Council's ("NRDC") Opening Brief, filed on August 5, 2015 in the above-captioned litigation.

7. 40 CFR § 155.53(c) states that EPA will provide a public comment period of "at least 30 calendar days" for draft risk assessments in the context of registration review. However, EPA's routine practice is and has been to provide at least 60 calendar days for such comment periods in order to provide sufficient time for thorough review and meaningful comments. EPA believes that public participation is critical for achieving transparency in the registration review decision-making process. Although the public participation process adds to the time frame for making reregistration decisions, particularly in complex or

controversial cases, the process leads to better decisions and more efficient use of Agency resources. In addition, the public benefits from the transparency and openness of the decision process. In developing the procedural regulations for the registration review program, EPA determined that taking public comment at key stages in the decision-making process was a key attribute for administering a credible registration review program.

8. In accordance with EPA's routine practice, the Agency intends to publish the draft risk assessment for TCVP in the Federal Register and provide a public comment period of at least 60 calendar days.

9. It is EPA's current intention and belief that the Agency will issue a final revised response to NRDC's April 23, 2009 Petition to Cancel All Pet Uses for the Pesticide Tetrachlorvinphos ("Petition") within 90 calendar days of issuing the final risk assessment in the context of the TCVP registration review.

10. EPA will not be in a position to estimate the amount of time needed to issue a final risk assessment in the context of the TCVP registration review, including a response to all comments received regarding the draft risk assessment, until after the close of the comment period for the draft risk assessment and EPA has at least preliminarily reviewed the comments. As a general matter, the greater the volume of comments received, and the greater the scientific complexity of the issues raised in those comments, the longer it takes to complete a final risk

assessment. However, I believe that the Agency would be in a position to estimate the amount of time needed to issue a final risk assessment and response to comments, and to communicate that estimate to NRDC, within 45 days after the close of the comment period.

In accordance with 28 U.S.C. § 1746, I declare under penalty of perjury that the foregoing is true and correct.

Executed this 29th day of September, 2015.

Richard P. Keigwin, Jr.

Exhibit K

U.S. ENVIRONMENTAL PROTECTION AGENCY

OFFICE OF INSPECTOR GENERAL

Chemical Safety

EPA Needs Policies and Procedures to Manage Public Pesticide Petitions in a Transparent and Efficient Manner

Report No. 16-P-0019 **October 27, 2015**

Report Contributors:

Heather Cursio
Jeffrey Harris
Kalpana Ramakrishnan
Thane Thompson

Abbreviations

ACUS	Administrative Conference of the United States
APA	Administrative Procedure Act
EPA	U.S. Environmental Protection Agency
FFDCA	Federal Food, Drug, and Cosmetic Act
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FY	Fiscal Year
NRC	Nuclear Regulatory Commission
NRDC	Natural Resources Defense Council
OAR	Office of Air and Radiation
OCSPP	Office of Chemical Safety and Pollution Prevention
OGC	Office of General Counsel
OIG	Office of Inspector General
OMB	Office of Management and Budget
OPP	Office of Pesticide Programs

Cover photo: A farmer in Watsonville, California, sprays crops with pesticides. (EPA photo)

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U.S. Environmental Protection Agency
Office of Inspector General

16-P-0019
October 27, 2015

At a Glance

EPA Needs Policies and Procedures to Manage Public Pesticide Petitions in a Transparent and Efficient Manner

Why We Did This Review

We evaluated the effectiveness of U.S. Environmental Protection Agency (EPA) processes used to track the receipt, disposition and resolution of public pesticide petitions. Specifically, we evaluated whether the EPA has processes to ensure transparency and consistency when responding to public pesticide petitions.

The EPA regulates pesticides under the Federal Insecticide, Fungicide, and Rodenticide Act and the Federal Food, Drug, and Cosmetic Act. Public petitions can be submitted to the Office of Pesticide Programs (OPP) for rulemaking; to modify or revoke pesticide tolerances; to cancel a pesticide's registration(s); or to request a specific action on a policy, guidance or agency process.

This report addresses the following EPA goals or cross-agency strategies:

- *Ensuring the safety of chemicals and preventing pollution.*
- *Embracing EPA as a high-performing organization.*

Send all inquiries to our public affairs office at (202) 566-2391 or visit www.epa.gov/oig.

The full report is available at: www.epa.gov/office-inspector-general/oig-reports.

What We Found

OPP does not have policies or procedures to ensure transparency when managing public pesticide petitions. Due to the lack of transparency and direct communication, some petitioners sued the EPA for "unreasonable delay," resulting in unnecessary costs to the agency and public. OPP did not effectively communicate with petitioners in the following manner:

OPP's lack of policies and procedures to manage public pesticide petitions in a transparent and efficient manner leaves petitioners unaware of petition status, which can result in unreasonable delay lawsuits costing the agency time and resources.

- Acknowledge petition receipt.
- Provide updates about the agency's work to resolve petitions.
- Provide petition decisions.

In addition, OPP lacks policies and procedures to manage petitions in a generally efficient or effective manner. Specifically:

- Petition documentation was not readily accessible, which was inconsistent with each of the EPA's Records Management Policies in place during the timeframe of our review.
- Some petition data were inaccurate, which resulted in the duplication of work to confirm data.
- According to OPP, petitions may take weeks to arrive at the correct office for action, because there is no guidance on how to submit petitions directly to OPP.
- OPP does not provide guidance to the public on how to submit complete petitions, which resulted in some petitioners providing supplemental information, and increased the time and resources to reach petition decisions.

By contrast, the EPA's Office of Air and Radiation and the Nuclear Regulatory Commission are considered to have best practices with policies and procedures for acknowledging petition receipt, directly communicating the petition decision to the petitioner, and tracking petitions.

Recommendations and Planned Agency Corrective Actions

We recommend that the Assistant Administrator for Chemical Safety and Pollution Prevention develop policies and procedures to manage public petitions in a transparent, effective, and efficient manner; communicate directly with petitioners; train staff to adhere to the Records Management Policy; implement an effective tracking system for public petitions; and provide guidance to the public on how to submit petitions with sufficient data for review. The EPA agreed with our recommendations and has proposed acceptable corrective actions. All recommendations are resolved. No further response from the agency is needed.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

THE INSPECTOR GENERAL

October 27, 2015

MEMORANDUM

SUBJECT: EPA Needs Policies and Procedures to Manage Public Pesticide Petitions in a Transparent and Efficient Manner
Report No. 16-P-0019

FROM: Arthur A. Elkins Jr.

TO: Jim Jones, Assistant Administrator
Office of Chemical Safety and Pollution Prevention

This is a report on the subject evaluation conducted by the Office of Inspector General (OIG) of the U.S. Environmental Protection Agency (EPA). This report contains findings that describe problems the OIG has identified and corrective actions the OIG recommends. This report represents the opinion of the OIG and does not necessarily represent the final EPA position. Final determinations on matters in this report will be made by EPA managers in accordance with established audit resolution procedures.

The EPA office having primary responsibility for the issues evaluated in this report is the Office of Chemical Safety and Pollution Prevention's Office of Pesticide Programs.

Action Required

In accordance with EPA Manual 2750, your office provided acceptable and complete planned corrective actions in response to OIG recommendations. All recommendations are resolved and no final response to this report is required.

We will post this report to our website at http://www.epa.gov/oig.

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Appendices

Purpose

The U.S. Environmental Protection Agency (EPA), Office of Inspector General (OIG), evaluated how the Office of Chemical Safety and Pollution Prevention (OCSPP) tracks the receipt, disposition and resolution of public petitions. This evaluation focused on OCSPP's Office of Pesticide Programs (OPP) and its policies and procedures used to ensure consistency and transparency when responding to pesticide-related public petitions.

Background

The EPA regulates pesticides under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). In summary, FIFRA defines a pesticide as any substance intended to destroy, prevent or repel pests, such as insects, weeds, fungi and rodents. FIFRA requires that pesticides produced, sold or distributed in the United States be registered by the EPA.

In addition to pesticide registration, the Federal Food, Drug, and Cosmetic Act (FFDCA) authorizes the EPA to set tolerances (maximum pesticide residue levels) of a pesticide allowed in or on food. The EPA must review and re-register pesticides every 15 years.[1]

The Public's Right to Petition

The public can submit pesticide petitions to the EPA under FIFRA, FFDCA, the Administrative Procedure Act (APA), or any combination of these authorities.

The APA requires agencies to respond to public petitions "within a reasonable time."

According to the APA, "each agency shall give an interested person the right to petition for the issuance, amendment, or repeal of a rule."[2] While the APA does not establish procedures for how agencies resolve petitions for rulemaking, it does require agencies to respond to public petitions "within a reasonable time."

FIFRA does not address how a person can petition the agency, whereas FFDCA states any person can file a petition for a regulation to modify a pesticide's tolerance with the Administrator. FIFRA does not set requirements for the EPA to respond to the petitioner within a specific timeframe. However, the petitioner can file a lawsuit, under the APA, claiming unreasonable delay if the petitioner finds the EPA has not responded within what the petitioner considers a reasonable amount of time.

---

[1] OPP is primarily a licensing office and receives many applications from pesticide manufacturers related to the issuance of pesticide registrations and the establishment of tolerances.

[2] The APA governs the federal rulemaking process. It establishes requirements for federal agencies to promulgate rules, such as requiring agencies to make information available to the public about new rules, and allowing the public to comment on notices of proposed rules.

OPP and the agency's Office of General Counsel (OGC) work together to respond to various types of public pesticide petitions (Table 1).

Table 1. Types of public petitions managed by OPP

Public petition	Actions requested
Registration	A petition from the public to cancel (terminate), suspend or modify a pesticide registration or registrations.
Rulemaking	A petition from the public to request the agency initiate an APA rulemaking to change the EPA's FIFRA pesticide regulations.
Policy	A petition from the public to request a specific action on a policy, guidance, or agency process.
Tolerance	A petition from the public to revoke or modify a pesticide tolerance or tolerances.

Source: EPA Office of General Counsel.

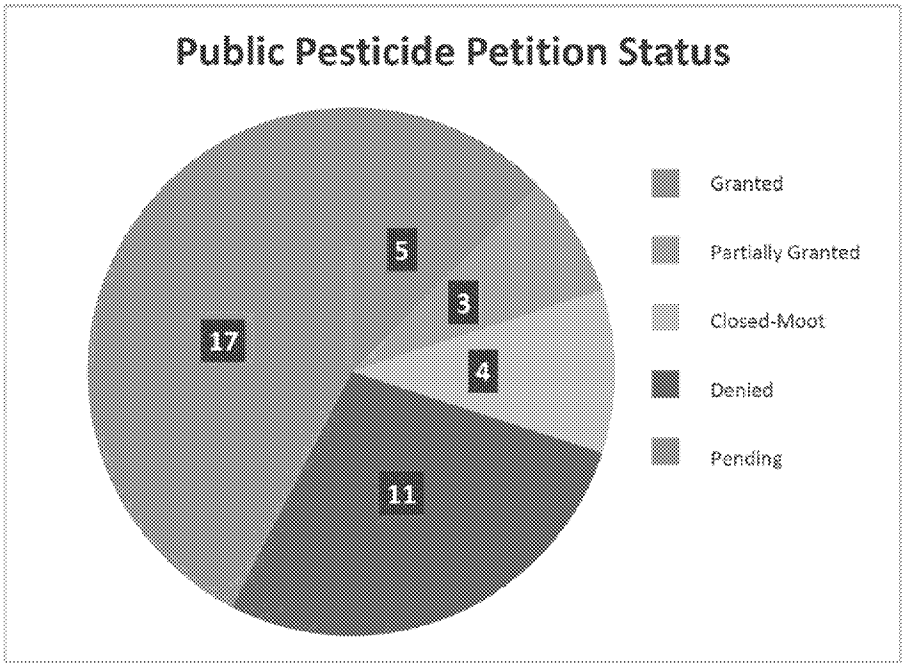
Petitions are received by the agency via mail, fax, email, or as online comments to ongoing pesticide regulatory work, such as a pesticide's registration review.[3] Public pesticide petitions can be directed to the EPA Administrator, sent directly to OPP and OGC officials, or sent to staff conducting assessments of the pesticide in question. When a public pesticide petition is received, both OPP and OGC assign staff to assess the scientific and legal requirements of the petition. When developing the final petition response, OPP and OGC work together to document a decision.

From fiscal years (FYs) 2005 through 2014, OPP received 40 public pesticide petitions that were submitted by members of the public. Most petitions addressed unique subjects, such as requests to revoke all tolerances, or to cancel or suspend specific pesticides. Some pesticide issues were the subject of more than one petition. OPP considered a petition closed/moot if the pesticide of interest was voluntarily canceled or the pesticide tolerance was revoked, rendering the petition "moot." Based on OPP's description of each petition's status, we categorized the status as granted, partially granted,[4] closed/moot, denied or pending (Figure 1).

[3] To initiate a new pesticide registration or an existing pesticide registration review, the EPA opens an online public docket that will house risk assessments and supporting documents. The EPA allows the public to review and comment on the online dockets. When public petitions to revoke a pesticide's tolerance are received as comments during the registration review process, OPP will typically open an online docket and publish a Notice of Receipt in the Federal Register.

[4] When a petition is partially granted, it can mean that other aspects of the petition were partially denied.

Figure 1: Status of the 40 public pesticide petitions submitted (FYs 2005–2014)[5]



Source: The EPA.

OPP determines whether the petition includes the necessary scientific information to make a decision. When petitioners ask the agency to assess a pesticide in advance of the designated registration review timeframe, OPP will incorporate the petition into its ongoing work, based on established priorities. Making a petition decision requires review of complex technical and scientific data, which can be a lengthy process.

Management's Responsibility to Promote Transparency and Efficient Use of Resources

The Administrative Conference of the United States (ACUS) provides recommendations and best practices pertaining to the management of petitions in a transparent and efficient manner.[6] In 2014, ACUS adopted recommendations from the *Petitions for Rulemaking* report,[7] which sets forth guidelines for agencies to follow when developing procedures for managing petitions.[8] Best practices to

[5] OPP verified petition data as of February 11, 2015.
[6] An independent federal agency, ACUS provides recommendations and nonpartisan expert advice about improving administrative procedures. According to its website, ACUS promotes, "improved government procedures including fair and effective dispute resolution and wide public participation and efficiency in the rulemaking process."
[7] Schwartz, Jason A. and Revesz, Richard L (2014), *Petitions for Rulemaking Final Report to the Administrative Conference of the United States*, New York University Law School.
[8] The *Petitions for Rulemaking* report is relevant to our evaluation because it provides best practices and recommendations for federal agencies managing formal requests from the public.

promote transparency and customer satisfaction include direct communication with petitioners to 1) acknowledge petition receipt, 2) provide status updates, and 3) provide petition decisions. Direct communication with petitioners throughout the petition process also reduces the risk of unreasonable delay lawsuits. Additionally, the *Petitions for Rulemaking* report recommends internal controls to promote efficiencies, such as using online platforms to educate the public about how to submit complete petitions and providing a point of contact for petition submissions.

The 2014 *Petitions for Rulemaking* report stated: "[O]ne of the biggest complaints among petitioners is that, after the agency sends an initial receipt and dockets the petition, the petition seems to enter a 'black hole': most agencies provide no regular updates and may disclose little about the petition's status even if the petitioner reaches out to them."

The EPA is responsible for managing its programs using internal controls, such as policies and procedures, to promote the efficient and effective use of resources. The Office of Management and Budget's (OMB's) Circular A-123 states that "[agency] management has a fundamental responsibility to develop and maintain effective internal control." Further, OMB policy indicates that internal control includes policies, procedures and organization to meet agency goals, and reports on agency operations.

Responsible Offices

The EPA office with primary responsibility for the issues evaluated in this report is the Office of Chemical Safety and Pollution Prevention's Office of Pesticide Programs. OGC also works in conjunction with OPP to determine petition requirements and draft the petition response.

Scope and Methodology

We conducted our work from November 2014 through August 2015. We conducted this performance audit in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objectives. We met with key OPP and OGC staff working on public pesticide petitions. We also met with other EPA program offices that manage public petitions (e.g., the Office of Solid Waste and Emergency Response, the Office of Air and Radiation and the Office of Pollution Prevention and Toxics).

From the 40 petitions received by OPP during the timeframe reviewed (FY 2005 though FY 2014), we randomly selected a sample of eight public petitions to determine the accuracy of petition information OPP managed and whether OPP

communicated directly with petitioners to acknowledge petition receipt, provide updates, or provide petition decisions. In addition, we also:

- Reviewed the prior EPA OIG Report No. 2006-P-0003, *Changes Needed to Improve Public Confidence in EPA's Implementation of the Food Quality Protection Act*, issued October 19, 2005.[9] In response to the report, OPP said it would post petition responses on an EPA website or the Federal Register website. OPP also agreed to communicate petition decisions directly to the petitioners in order to increase transparency of the agency's work.[10]

- Reviewed the 2014 *Petitions for Rulemaking* report. The 2014 report assessed how federal agencies, including the EPA, processed formal rulemaking requests from the public and provided recommendations on how to improve the petition process.[11]

- Met with one federal agency, the Nuclear Regulatory Commission (NRC), described in the *Petitions for Rulemaking* report as having best practices when responding to public petitions.

- Met with one stakeholder, the Natural Resources Defense Council (NRDC), which filed 11 of the 40 public petitions received by OPP during the timeframe reviewed.[12]

Results of Review

OPP does not have internal controls to manage public pesticide petitions in a transparent manner and does not effectively communicate with petitioners, which resulted in unreasonable delay lawsuits, costing petitioners and the agency time and resources. In our detailed analysis of eight petitions, we found OPP did not communicate directly in any instances with petitioners by sending letters acknowledging petition receipt. Further, OPP did not communicate updates of the EPA's ongoing work for five petitions, and four petitioners did not receive direct communication of the agency's petition decisions. The lack of transparency and direct communication with petitioners resulted in unreasonable delay lawsuits.

We also found that OPP lacks internal controls to manage petitions in an efficient and effective manner. OPP's petition documentation was not readily accessible, which is inconsistent with each of the EPA's Records Management Policies in place during the timeframe of our review. OPP informally tracks the status of

[9] http://www.epa.gov/oig/reports/2006/20051019-2006-P-00003.pdf.
[10] According to the EPA's audit tracking system, all recommendations have been fulfilled by OPP.
[11] The *Petitions for Rulemaking* report included an assessment of 26 federal agencies and 18 external stakeholders that were interviewed and/or responded to questionnaires concerning their perspectives on rulemaking petitions.
[12] NRDC submitted 11 public pesticide petitions to OPP from FYs 2005 through 2014; seven petitions were submitted independently by the NRDC, and four petitions were submitted in conjunction with other organizations.

some petitions, but we found the petition data were inaccurate. In addition, OPP lacks policies or procedures to provide the public guidance on how to submit a petition directly to its office, or how to submit a complete petition. Poor record-keeping practices, and the lack of guidance concerning how to submit petitions, create resource inefficiencies.

OPP Has No Policies or Procedures for Managing Public Petitions

OPP does not have policies or procedures to ensure a consistent and transparent process to support the efficient use of EPA resources when managing public pesticide petitions.[13] Specifically, OPP does not have policies or procedures for:

- Communicating directly with petitioners, such as:
  - Acknowledging petition receipt directly with the petitioners.
  - Posting a Notice of Receipt to an appropriate website.
  - Providing petitioners with updates on the EPA's work to resolve the petition.
  - Sending petition decisions directly to the petitioner, along with posting the decision to an appropriate website.
- Ensuring staff are trained to manage petition documentation so that the information can be retrieved in a timely manner.
- Tracking petitions in a formal and consistent manner.
- Providing the public with guidance for submitting petitions directly to OPP, and directions for submitting a complete petition with sufficient data for review.

Effective Communication With Petitioners Does Not Occur

The 2014 *Petitions for Rulemaking* report stated: "Stakeholders may anticipate that costly and unpredictable litigation over unreasonable delay would end up being necessary to prompt an agency to respond to a petition."

In our review of eight petitions, we found that OPP did not effectively communicate petition receipt, status of petition review, or petition decisions directly to petitioners. NRDC stakeholders we interviewed said direct communication with petitioners, starting with acknowledgment of petition receipt, is important and would reduce risk of unreasonable delay lawsuits and increase stakeholder confidence. Among our sample of eight petitions, OPP was unable to provide documentation that it communicated directly with petitioners to acknowledge petition receipt for any of the eight petitions. OPP said it may have

[13] In contrast, OPP has procedures in place to manage petitions submitted by industry applicants to modify a pesticide's tolerance. For example, OPP has procedures to receive and review industry tolerance petitions, prepare a Notice of Receipt for inclusion in the Federal Register, post decisions in the Federal Register, and maintain records of petitions submitted by industry applicants.

contacted petitioners to acknowledge petition receipt, but OPP did not have documentation.

OPP did not provide evidence of direct communication during the petition review process for five of eight petitions in our sample. OPP sent letters directly to one petitioner in our sample, providing partial responses and information about the EPA's ongoing work. However, OPP sent its letter almost 5 years after the petition was submitted, and only after the petitioner filed a lawsuit for unreasonable delay. In an effort to promote transparency with petitioners, OPP created public online dockets for four petitions in our sample, but not all petition information was available for review. In addition, OPP noted that it disseminates petition information through public meetings, online dockets, and flash news alerts posted on EPA websites.[14]

Among the 40 public petitions received by OPP from FYs 2005 through 2014, nine were associated with unreasonable delay lawsuits. The NRDC is responsible for initiating most of these (seven of nine, or 78 percent). NRDC stakeholders we interviewed stated that if the EPA had directly communicated petition status updates, they might not have initiated lawsuits.

During the review of petitions in our sample, we found that petition decisions are inconsistently communicated directly to the petitioner. In our sample of eight petitions,[15] only three petition decisions were mailed directly to petitioners. NRDC stakeholders said that although they are sometimes aware that EPA petition-related work could be available in online dockets, it is not always clear if the work was conducted in response to the stakeholder's petition.

Records Management Requirements Are Not Met

The EPA's records management policies establish principles, responsibilities and requirements for managing agency records in compliance with federal laws and regulations. Each of the policies require that data be maintained in such a way to allow for easy or timely access and retrieval. For the eight petitions we reviewed, OPP staff were unable to quickly or easily retrieve petition documentation. In some cases, this was because the staff who worked most closely with the petition were no longer working with the agency.

Updated in February 2015, the EPA's Records Management Policy states each office within the EPA must establish and maintain a records management program, which includes a requirement to, "maintain records so they can be accessed by staff with a need to know the information for appropriate business reasons and maintained for the required retention period." The Records

[14] NRDC stakeholders stated that posting information to public online websites is not the same as direct communication with the petitioner, because the petitioner could be unaware that the petition is being addressed in the online posting.
[15] In our sample of eight petitions, seven petitions were resolved; one was still pending.

Management Policy also states that all employees transferring or leaving the agency identify and transfer records to another EPA employee.

Petition Tracking Data Were Inaccurate

During our review, we found several instances where the petition data initially provided by OPP were inaccurate concerning status, date of petition resolution, the statute under which the petition was submitted, or litigation record. We asked OPP and OGC to review their original petition data. Table 2 notes where OPP made changes to the original petitions information after we requested additional agency review.

Table 2: Agency corrections made to petition status due to OIG review

Status of public pesticide petitions	Initial OPP petition status	Corrected OPP petition status
Granted	2	5
Partially granted	4	3
Closed/moot	3	4
Denied	11	11
Pending	17	17
Unknown	3	0
Total	40	40

Source: The EPA.

When we requested OPP to reconfirm the petition tracking data provided to us, OPP and OGC changed the status of three petitions from pending to resolved,[16] and the status of another two petitions changed from resolved to pending. OPP currently tracks petitions to revoke tolerances manually via a chart, but it does not have a policy to track the status of public petitions. Inaccurate petition status tracking resulted in the duplication of work and inefficient use of resources.

OPP Does Not Provide Guidance on How to Submit Public Petitions

OPP does not provide guidance on how to submit a public petition directly to its office, or how to submit a petition that provides sufficient data for review. According to the OGC, when petitions are sent only to the Office of the Administrator, it may take weeks before the petition arrives at OPP for action. OPP stated that because every petition is unique, the office does not have uniform processes for how petitions are received or routed through the agency. Moreover, OPP does not provide a point of contact for public petition submissions.

In addition, OPP does not provide guidance on what information must be submitted to ensure a petition is complete and has sufficient data for review. OPP noted that the petition review process is resource intensive, especially

[16] Resolved indicates a petition was granted, partially granted, closed/moot or denied.

when petitions do not have sufficient data for review. Both OPP and OGC said petitioners can submit supplemental information or amendments to petitions, but both offices believe this practice can impact OPP's ability to resolve petitions in a timely manner. If petitioners receive guidance on how to submit public pesticide petitions with adequate data, the time and resources required to reach petition decisions could be reduced.

Best Practices for Managing Petitions

We documented best practices for managing petitions in another EPA office and federal agency. The EPA's Office of Air and Radiation (OAR) has internal controls to manage its petitions and prioritize transparency and efficiency. OAR sends letters acknowledging receipt of a petition, directly communicates the petition decision to the petitioner, and announces the decision in the Federal Register. The OAR also tracks petitions.

The *Petitions for Rulemaking* report recognized the Nuclear Regulatory Commission for numerous best practices when responding to rulemaking petitions.[17] During our interview, we also confirmed that the NRC:

- Sends a letter to the petitioner acknowledging the receipt of a petition.
- Communicates with the petitioner if necessary.
- Places rulemaking petitions in online dockets for public access.
- Sends a letter to the petitioner with a notification of the petition decision.
- Publishes the petition decision in the Federal Register.

The NRC also has formal processes to manage petition resolution and maintains a comprehensive petition website detailing approximately 100 regulatory petitions received over the past 10 years. Adopting similar best practices would help the EPA improve its petition management processes.

Conclusion

OPP's lack of policies and procedures to manage public pesticide petitions in a transparent and efficient manner resulted in unreasonable delay lawsuits, duplication of work, and reduced customer satisfaction. The agency will reduce the risk of unreasonable delay lawsuits by effectively communicating with petitioners about petitions received, provide status updates, and provide petition decisions. OPP can reduce errors in its petitions tracking data by effectively tracking public petitions. OPP can also improve its record-keeping practices and adherence to the EPA's Records Management Policy.

Providing guidance to the public concerning how to submit a petition directly to OPP will reduce delays in OPP's receipt and subsequent action on a petition. In addition, providing guidance to the public concerning information the agency

[17] The NRC stated the timeline to provide a response is "within 3 months."

considers necessary or sufficient in a petition supports higher quality petition submissions. Such guidance can also reduce the EPA's petition review and response time, and increase customer satisfaction.

Recommendations

We recommend that the Assistant Administrator for Chemical Safety and Pollution Prevention:

1. Develop policies and standard operating procedures to manage public petitions received by OPP in a transparent and efficient manner. These procedures should include direct communication with petitioners by:

    a. Providing a letter to the petitioner acknowledging receipt of the petition.
    b. Communicating petition decisions to the petitioner in writing.
    c. Providing updates to petitioners about the status and progress of pending petitions.

2. Train staff managing public pesticide petitions to adhere to the EPA's Records Management Policy.

3. Develop and implement an effective petition tracking system for public pesticide petitions.

4. Provide criteria and guidelines for submission of public pesticide petitions that provide sufficient information for EPA review.

Agency Comments and OIG Evaluation

The agency agreed with our recommendations, and provided corrective actions and estimated completion dates that meet the intent of the recommendations. All recommendations are resolved. No further response to this report is required. The agency's detailed response is found in Appendix A.

Status of Recommendations and Potential Monetary Benefits

RECOMMENDATIONS						POTENTIAL MONETARY BENEFITS (in $000s)	
Rec. No.	Page No.	Subject	Status[1]	Action Official	Planned Completion Date	Claimed Amount	Agreed-To Amount
1	10	Develop policies and standard operating procedures to manage public petitions received by OPP in a transparent and efficient manner. These procedures should include direct communication with petitioners by: a. Providing a letter to the petitioner acknowledging receipt of the petition. b. Communicating petition decisions to the petitioner in writing. c. Providing updates to petitioners about the status and progress of pending petitions.	O	Assistant Administrator for Chemical Safety and Pollution Prevention	10/2016		
2	10	Train staff managing public pesticide petitions to adhere to the EPA's Records Management Policy.	O	Assistant Administrator for Chemical Safety and Pollution Prevention	11/2016		
3	10	Develop and implement an effective petition tracking system for public pesticide petitions.	O	Assistant Administrator for Chemical Safety and Pollution Prevention	10/2016		
4	10	Provide criteria and guidelines for submission of public pesticide petitions that provide sufficient information for EPA review.	O	Assistant Administrator for Chemical Safety and Pollution Prevention	10/2017		

[1] O = Recommendation is open with agreed-to corrective actions pending.
C = Recommendation is closed with all agreed-to actions completed.
U = Recommendation is unresolved with resolution efforts in progress.

Appendix A

Agency Response to Draft Report

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

MEMORANDUM

SUBJECT: Comments on OIG Draft Report "EPA Needs Policies and Procedures to Manage Public Pesticide Petitions in a Transparent and Efficient Manner," Project No. OPE-FY15-0004

FROM: James J. Jones
Assistant Administrator

TO: Arthur A. Elkins, Jr.
Inspector General

This memorandum is in response to the Office of Inspector General's (OIG) Draft Report entitled "EPA Needs Policies and Procedures to Manage Public Pesticide Petitions in a Transparent and Efficient Manner" (August 3, 2015). The Office of Chemical Safety and Pollution Prevention (OCSPP) appreciates the OIG's effort in evaluating the effectiveness of EPA's processes used to track the receipt, disposition, and resolution of public pesticide petitions. OCSPP agrees with the OIG's four recommendations. Accordingly, our response includes our proposed corrective actions and a timeframe for their implementation.

I. Background

As the OIG's analysis revealed, OCSPP's Office of Pesticide Programs (OPP) processes several different types of "petitions" in the normal course of its regulatory business. By far the most numerous of these are petitions for tolerance actions. Under section 408(d) of the FFDCA, any person can file a petition proposing the issuance of a regulation establishing, modifying, or revoking (a) a tolerance for a pesticide chemical residue in or on food, or (b) an exemption from the requirement to have a tolerance for such residue.

Petitions for tolerance actions must comply with the procedures detailed in 40 CFR §180.7(a) – (d). Such petitions generally fall into one of the four categories listed below:

- Petition to establish a new tolerance
- Petition to amend a codified tolerance
- Petition to revoke a codified tolerance
- Petition to establish an exemption from the requirement for a tolerance

Under 40 CFR §180.7(e) – (h), the Agency follows well established procedures for tracking, processing, and providing updates (online) to petitioners for tolerance actions. OPP receives and processes over a hundred tolerance action petitions annually. However, OPP also receives a much smaller number of other requests for Agency action, for which OPP does not currently have comprehensive procedures. These requests include:

- Petitions to promulgate regulations under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and the Administrative Procedures Act (APA); and
- Petitions to take non-rule, regulatory actions under FIFRA (e.g., cancellation of pesticide registrations).

OCSPP agrees with the OIG recommendations that the Agency needs to standardize operating procedures to manage the latter category of public petitions in a more transparent manner.

OIG Response: OPP has procedures in place to manage tolerance petition actions submitted by industry applicants, as noted above. This evaluation did not address requests for action related to individual pesticide products and tolerances received from the pesticide industry (or other persons, such as growers or food importers, seeking the establishment of a tolerance). Instead, the focus of this evaluation was primarily on petitions for actions OPP receives from members of the public to revoke a tolerance. These petitions may ask the EPA to exercise its statutory authority to cancel or suspend the registrations of the pesticide that is the subject of the tolerance revocation petition.

II. OCSPP Responses to OIG's Recommendations

Recommendation 1: The Assistant Administrator for Chemical Safety and Pollution Prevention should develop policies and standard operating procedures to manage public petitions received by the OPP in a transparent and efficient manner. These procedures should include:

1. Direct communication with petitioners by:
    a. Providing a letter to the petitioner acknowledging receipt of the petition.
    b. Communicating petition decisions to the petitioner in writing.
    c. Providing updates to petitioners about the status and progress of pending petitions.

OCSPP Response:
OCSPP agrees with this recommendation. The program will develop appropriate policies and standard operating procedures (SOPs) to manage public petitions received by OPP in a transparent and efficient manner. The procedures will include the direct communication protocols listed in the OIG's recommendation. Estimated date of completion: October 2016.

Recommendation 2:
Train staff managing public pesticide petitions to adhere to the EPA's current Records Management Policy.

OCSPP Response:
OCSPP agrees with this recommendation. The standard operating procedures described in Corrective Action 1 will address maintaining appropriate records for covered petitions. When the SOP is final, OPP will issue a memo informing appropriate staff and management of their responsibilities for maintaining these records, and directing the use of the SOPs to meet their responsibilities under the Agency's Records Management Policy. Estimated date of completion: November 2016.

Recommendation 3:
Develop and implement an effective petition tracking system for public pesticide petitions.

OCSPP Response:
OCSPP agrees that OPP does not have a formal tracking system specifically for pesticide petitions not covered by 40 CFR §180.7, such as petitions seeking FIFRA/APA rulemaking or cancellation of registrations. The standard operating procedures described in Corrective Action 1 will include procedures for tracking these petitions. Estimated date of completion: October 2016.

Recommendation 4: Provide criteria and guidelines for submission of public pesticide petitions that provide sufficient information for EPA review.

OCSPP Response:
OCSPP agrees, and commits to develop and post to the Agency Pesticides website criteria and guidelines for public submission of pesticide petitions not covered by 40 CFR §180.7. Estimated date of completion: October 2017.

III. Contact Information:

If you have any questions regarding this response, please contact Janet L. Weiner, OCSPP's Audit Liaison at (202) 564-2309.

Appendix B

Distribution

Office of the Administrator
Assistant Administrator for Chemical Safety and Pollution Prevention
Agency Follow-Up Official (the CFO)
Agency Follow-Up Coordinator
General Counsel
Associate Administrator for Congressional and Intergovernmental Relations
Associate Administrator for Public Affairs
Deputy Assistant Administrator for Chemical Safety and Pollution Prevention
Director, Office of Pesticide Programs, Office of Chemical Safety and Pollution Prevention
Director, Office of Pollution Prevention and Toxics, Office of Chemical Safety and Pollution Prevention
Deputy Director for Management, Office of Pesticide Programs, Office of Chemical Safety and Pollution Prevention
Deputy Director for Programs, Office of Pesticide Programs, Office of Chemical Safety and Pollution Prevention
Audit Follow-Up Coordinator, Office of Chemical Safety and Pollution Prevention
Audit Follow-Up Coordinator, Office of Pesticide Programs, Office of Chemical Safety and Pollution Prevention
Audit Follow-Up Coordinator, Office of Pollution Prevention and Toxics, Office of Chemical Safety and Pollution Prevention

Exhibit L

No. 15-70025

UNITED STATES COURT OF APPEALS
FOR THE NINTH CIRCUIT

NATURAL RESOURCES DEFENSE COUNCIL, INC.,

Petitioner,

v.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY,

Respondent.

RESPONDENT'S RENEWED MOTION FOR VOLUNTARY REMAND

On September 25, 2015, Respondent United States Environmental Protection Agency ("EPA" or "Agency") moved for voluntary remand of its November 6, 2014 response to Petitioner Natural Resources Defense Council's ("NRDC") April 23, 2009 Petition Requesting Cancellation of All Pet Uses of Tetrachlorvinphos ("Response to the Cancellation Petition") on the grounds that EPA is preparing a new risk assessment for tetrachlorvinphos that could moot or narrow the issues in this litigation. Dkt. 22. On December 16, 2015, this Court denied the motion without prejudice and stated that EPA could renew its motion for voluntary remand after the Agency "issued a new draft risk assessment." Dkt.

25. On December 21, 2015, EPA issued the Draft Human Health Risk Assessment for Tetrachlorvinphos ("Draft Risk Assessment").[1] The Draft Risk Assessment was published in the Federal Register on January 20, 2016, opening a 60-day public comment period. *See* 81 Fed. Reg. 3128 (Jan. 20, 2016). Accordingly, EPA hereby renews its motion for voluntary remand pursuant to Federal Rule of Appellate Procedure 27 and this Court's December 16, 2015 Order. Counsel for NRDC have represented that NRDC opposes a voluntary remand that is not accompanied by vacatur of the underlying decision.

The Draft Risk Assessment differs in several ways from the prior risk assessment relied upon by EPA in responding to NRDC's petition. Thus, EPA intends to revisit its prior response in light of the new risk assessment. EPA's reevaluation of its Response to the Cancellation Petition could moot or significantly narrow the issues raised by NRDC in this litigation, and remand would best serve the interests of judicial economy.

BACKGROUND

The Federal Insecticide, Fungicide, and Rodenticide Act ("FIFRA"), 7 U.S.C. §§ 136-136y, requires EPA approval of pesticides prior to their distribution

[1] The 152-page Draft Risk Assessment is available at http://www.regulations.gov/contentStreamer?documentId=EPA-HQ-OPP-2008-0316-0036&disposition=attachment&contentType=pdf.

or sale, and establishes a registration regime for regulating the use of pesticides. 7 U.S.C. § 136a(a), (c). EPA must approve an application for pesticide registration if, among other things, the pesticide will not cause unreasonable adverse effects on the environment. *Id.* § 136a(c)(5). Section 3(g) of FIFRA, 7 U.S.C. § 136a(g), requires EPA to periodically reevaluate pesticides through a process known as "registration review" in order to ensure that they continue to meet the standards for registration.

Tetrachlorvinphos is a member of the organophosphate class of pesticides that act by inhibiting the enzyme acetylcholinesterase. Tetrachlorvinphos was first registered in 1966 and is primarily used on livestock and pets to control insects like fleas. In 2006, EPA reregistered tetrachlorvinphos after conducting a residential risk assessment for exposures to tetrachlorvinphos and a cumulative risk assessment for exposures to all organophosphates.[2] *See* Response to Cancellation Petition at 2.[3]

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[2] The process EPA uses for evaluating the potential for health and ecological effects of a pesticide is called risk assessment, which is part of a risk management process. In registration review, that risk assessment includes an ecological risk assessment, a human health risk assessment, and, when appropriate, a cumulative risk assessment (evaluating the risk of a toxic effect to humans associated with concurrent exposure by all relevant non-occupational pathways and routes of exposure to a group of chemicals that share a common mechanism of toxicity).

[3] The Response to the Cancellation Petition is attached to NRDC's Petition for Review [Dkt. 1-2].

On April 23, 2009, NRDC petitioned EPA to cancel all pet uses for tetrachlorvinphos, arguing, among other things, that EPA's tetrachlorvinphos risk assessment failed to take into account exposures from pet collars. *See* Ptr.'s Br., ER58-ER63 [Dkt. 16-3]. In response to NRDC's 2009 petition, EPA conducted a residential risk assessment of the pet uses of tetrachlorvinphos (including pet collars) using the most recent science policies and methodologies available at the time. As explained in the Agency's Response to the Cancellation Petition, EPA concluded in its risk assessment that the potential risks of exposure to tetrachlorvinphos from pet products were below the Agency's level of concern. *See* Response to Cancellation Petition at 4-12. EPA relied on this risk assessment, among other things, when the Agency denied NRDC's request to cancel all pet uses of tetrachlorvinphos on November 6, 2014.

As part of its ongoing registration review for tetrachlorvinphos and other organophosphate pesticides, EPA's Office of Pesticide Programs is conducting a new risk assessment for all uses (not just pet uses) of tetrachlorvinphos. Declaration of Richard Keigwin, Jr., ¶ 4 ("Keigwin Decl.") [Dkt. 22-2]. Although this risk assessment is being conducted as part of an ongoing registration review and independently from this litigation, EPA is considering many of the scientific issues raised in this litigation in preparing the risk assessment. *Id.* ¶ 6.

EPA issued a draft of the new Human Health Risk Assessment on December 21, 2015, along with a more detailed Occupational and Residential Exposure Assessment and a memorandum responding to each of the arguments NRDC raised in its opening brief.[4] A notice of availability of the Draft Risk Assessment was published in the Federal Register on January 20, 2016, and EPA is accepting comments on the Draft Risk Assessment until March 21, 2016. 81 Fed. Reg. at 3128. Once EPA considers any public comments submitted, the Agency will finalize the risk assessment. Keigwin Decl. ¶ 10. EPA then intends to issue a revised response to NRDC's 2009 petition, considering the new final risk assessment for tetrachlorvinphos, within 90 days of finalizing that new assessment. *Id.* ¶ 9.

The December 21 Draft Risk Assessment differs in a number of ways from the earlier risk assessment relied upon by EPA in responding to NRDC's petition. Most notably, the Draft Risk Assessment retains the presumptive tenfold margin of safety identified in section 408(b)(2)(C) of the Federal Food, Drug, and Cosmetic

[4] The 124-page Occupational and Residential Exposure Assessment is available at http://www.regulations.gov/contentStreamer?documentId=EPA-HQ-OPP-2008-0316-0038&disposition=attachment&contentType=pdf. The memorandum, entitled "Tetrachlorvinphos (TCVP): Responses to Arguments Presented in the Natural Resources Defense Council, Inc.'s (NRDC) Aug. 5, 2015 Opening Brief in *NRDC v. EPA*, Case No. 15-70025 (9th Cir.)," is available at http://www.regulations.gov/contentStreamer?documentId=EPA-HQ-OPP-2009-0308-0014&disposition=attachment&contentType=pdf.

Act, 21 U.S.C. § 346a(b)(2)(C); this tenfold safety factor was not retained in EPA's earlier assessment.[5] *See, e.g.*, Draft Risk Assessment at 4, 27. The issue of whether the tenfold safety factor should have been retained in the earlier assessment is an important issue raised by NRDC in this case. *See* Ptr.'s Br. at 37-46. As explained in EPA's Reply in Support of its Motion for Voluntary Remand, the Agency has continued to evaluate over the last year whether the tenfold safety factor should be applied to *the entire class* of organophosphate pesticides. *See* Dkt. 24 at 3-4. EPA now recommends retaining the safety factor for the risk assessments of 30 different pesticides, only one of which is tetrachlorvinphos. *Id.* (citing EPA, "Literature Review on Neurodevelopment Effects & FQPA Safety Factor Determination for the Organophosphate Pesticides" (Sept. 25, 2015)).

ARGUMENT

"A reviewing court has inherent power to remand a matter to the administrative agency." *Loma Linda Univ. v. Schweiker*, 705 F.2d 1123, 1127 (9th Cir. 1983) (citation omitted). "[I]t is generally accepted that in the absence of a specific statutory limitation, an administrative agency has the inherent authority to

[5] The Food Quality Protection Act, which amended FIFRA and the Federal Food, Drug, and Cosmetic Act in 1996, requires EPA to apply "an additional tenfold margin of safety" to protect against harm to infants and children, unless EPA has "reliable data" that a different margin of safety "will be safe for infants and children." 21 U.S.C. § 346a(b)(2)(C).

reconsider its decisions." *Macktal v. Chao*, 286 F.3d 822, 825-26 (5th Cir. 2002) (citation omitted); *Trujillo v. Gen. Elec. Co.*, 621 F.2d 1084, 1086 (10th Cir. 1980) (noting that "the power to decide in the first instance carries with it the power to reconsider") (citation omitted). This authority includes the right to seek voluntary remand of a challenged agency decision, without confessing error. *SKF USA Inc. v. United States*, 254 F.3d 1022, 1029 (Fed. Cir. 2001).

While the reviewing court has discretion on whether to remand, voluntary remand is appropriate where the request is reasonable and timely. *Macktal*, 286 F.3d at 826. "Administrative reconsideration is a more expeditious and efficient means of achieving adjustment of agency policy than is resort to the federal courts." *B.J. Alan Co. v. ICC*, 897 F.2d 561, 562 n.1 (D.C. Cir. 1990) (*quoting Commonwealth of Pa. v. ICC*, 590 F.2d 1187, 1194 (D.C. Cir. 1978)). "Generally, courts only refuse voluntarily requested remand when the agency's request is frivolous or made in bad faith." *Cal. Cmtys. Against Toxics v. EPA*, 688 F.3d 989, 992 (9th Cir. 2012) (citation omitted).

Here, EPA is conducting a new assessment of the potential risks of exposure to tetrachlorvinphos with the benefit of scientific policies and methodologies that have evolved since the Agency's 2014 Response to the Cancellation Petition. As part of that new assessment, EPA has decided to retain the children's tenfold safety factor. EPA is also addressing the other major concerns raised by NRDC in this

proceeding. For example, as explained in its December 21, 2015 Memorandum addressing NRDC's arguments, EPA is considering using the "Davis study" supported by NRDC, and submitted the study to the Human Studies Review Board ("HSRB") to obtain the HSRB's recommendation as to the study's scientific validity and the ethical conduct of the study, as required by 40 C.F.R. § 26.1706.[6] Based on the new risk assessment, EPA intends to reevaluate NRDC's petition and revise its Response to the Cancellation Petition as appropriate.[7]

Remand of EPA's Response to the Cancellation Petition will serve the interests of judicial economy by possibly mooting or significantly narrowing the issues that NRDC has raised in this litigation. Additionally, remand will serve to improve the record, as EPA's renewed response to the arguments raised by NRDC

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[6] The HSRB is a federal advisory committee operating under the Federal Advisory Committee Act that provides advice, information, and recommendations on issues related to scientific and ethical aspects of research involving human subjects. The HSRB reports to the EPA Administrator through EPA's Office of the Scientific Advisor. In this case, the HSRB considered the "Davis study" during a public meeting on January 12-13, 2016. *See* http://www.epa.gov/osa/January-12-13-2016-meeting-human-studies-review-board. EPA expects that the meeting minutes will be posted publicly in February 2016 and to receive the final report from the HSRB on March 30, 2016.

[7] Although EPA intends to reevaluate NRDC's petition based on new scientific understanding, EPA does not concede that it erred in denying NRDC's petition based on the record before it at the time of the decision.

in its petition for cancellation of the pet uses of tetrachlorvinphos will be informed by the conclusions reached in the new risk assessment.

Granting this motion additionally promotes efficiency because remand is the ultimate outcome that NRDC seeks in this litigation. *See* Ptr.'s Br. at 71 ("[T]he case should be remanded to EPA to cancel the registrations for TCVP pet products or adequately explain why refusing to do so does not result in unreasonable adverse effects to children's health."). Thus, even if NRDC prevailed in its challenge to EPA's 2014 action—an action that is being reconsidered by EPA—there would still need to be further administrative proceedings regarding whether any cancellation of the registrations is warranted, and it would be EPA's responsibility to set a reasonable timetable for responding to NRDC's petition on remand.[8] EPA is simply proposing to move forward with remand now, rather than consuming judicial and governmental resources litigating over an earlier decision that EPA is already in the process of administratively reconsidering. Denying EPA's motion for voluntary remand would just compel EPA to devote limited resources to this litigation, as opposed to completing the ongoing scientific review process.

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[8] Mandamus is the appropriate remedy for any unreasonable agency delay. *See, e.g., NRDC v. EPA*, 489 F.3d 1364, 1375 (D.C. Cir. 2007). *See also Int'l Union, United Mine Workers of Am. v. Dep't of Labor*, 554 F.3d 150, 155 (D.C. Cir. 2009) (declining to impose schedule on remand).

EPA intends to conclude reconsideration of NRDC's petition within a reasonable period of time. Specifically, EPA intends to issue a revised response to NRDC's petition within 90 days after finalizing the risk assessment. While EPA cannot determine how long it might take to issue a final risk assessment until it sees the volume and complexity of public comments that may be submitted in response to the Draft Risk Assessment, EPA will be able to provide an estimate of how much time it might take to complete the final assessment within 45 days of the close of the comment period. Keigwin Decl. ¶ 10.

In short, remand would promote judicial and governmental economy by possibly mooting or significantly narrowing the issues that NRDC has raised in this litigation, and by facilitating the Agency's ability to devote its limited resources to completing the scientific review process rather than to this litigation.

CONCLUSION

For the foregoing reasons, EPA respectfully requests that the Court remand the Response to the Cancellation Petition to the Agency for further consideration.

Dated: February 11, 2016

Respectfully submitted,

JOHN C. CRUDEN
Assistant Attorney General
Environment & Natural Resources Division

s/ *Erica M. Zilioli*
ERICA M. ZILIOLI
U.S. Department of Justice
Environmental Defense Section
P.O. Box 7611
Washington, DC 20044
Telephone: (202) 514-6390
Facsimile: (202) 514-8865
Erica.Zilioli@usdoj.gov

Of Counsel:

BENJAMIN WAKEFIELD
Office of General Counsel
U.S. Environmental Protection Agency
William Jefferson Clinton Building North
1200 Pennsylvania Avenue, N.W.
Washington, DC 20460

Exhibit M

No. 15-70025

IN THE

United States Court of Appeals
For The Ninth Circuit

NATURAL RESOURCES DEFENSE COUNCIL, INC.,

Petitioner,

v.

U.S. ENVIRONMENTAL PROTECTION AGENCY,

Respondent.

On Petition for Review of an Order of the
U.S. Environmental Protection Agency

PETITIONER NATURAL RESOURCES DEFENSE COUNCIL'S RESPONSE TO RENEWED MOTION FOR VOLUNTARY REMAND; REQUEST FOR VACATUR AND REMAND

Mae Wu
NATURAL RESOURCES DEFENSE COUNCIL
1152 15th Street, NW, Suite 300
Washington, DC 20005
Telephone: (202) 289-6868
mwu@nrdc.org

Susannah Landes Weaver
Ian Fein
Kelsi Brown Corkran
ORRICK, HERRINGTON & SUTCLIFFE LLP
1152 15th Street, NW
Washington, DC 20005
Telephone: (202) 339-8400
Facsimile: (202) 339-8500
sweaver@orrick.com

Counsel for Petitioner

Almost seven years ago, Petitioner Natural Resources Defense Council ("NRDC") filed an administrative petition requesting that Respondent Environmental Protection Agency ("EPA") discontinue the use of a dangerous chemical pesticide in household pet products like flea collars. NRDC demonstrated that these products pose significant health risks to children who are exposed to the pesticide when they play with their pets. After waiting more than five years for EPA to respond and ultimately deny the petition, NRDC exercised its statutory right to ask this Court to review and set aside EPA's decision. But soon after NRDC filed its opening brief, EPA belatedly announced that it wanted to reassess the risks posed by the pesticide, and so asked this Court to refrain from reviewing its earlier decision and to allow it to dispose of NRDC's appeal through a voluntary remand instead. EPA has since issued a new draft risk assessment that admits these dangerous products may endanger children's health.

Because EPA's new draft risk assessment so thoroughly undermines the basis of its prior decision, NRDC is not opposed in principle to a remand at this time. Indeed, by reversing position on a crucial underlying safety factor, and acknowledging the importance of

key information that EPA previously ignored, the new draft risk assessment effectively confirms that EPA's earlier decision was not supported by substantial evidence.

However, any remand must—as a matter of basic fairness, and consistent with this Court's relevant precedents—be accompanied by vacatur of EPA's challenged decision as well.[1] If EPA is not willing to defend its prior decision, and NRDC is denied its right to have this Court review and set aside that decision on the merits, then EPA should not be allowed to leave that decision in force during a potentially lengthy remand. While this Court may remand without vacatur in the rare circumstance when equity "demands" that it do so, vacating EPA's decision here would cause no disruptive consequences at all.

If EPA wants a do-over—especially after waiting so long to make its earlier decision—then the Court should vacate the challenged denial order that EPA is no longer willing to defend. And at the very least, the Court should impose a deadline on the remand to ensure that EPA expeditiously resolves the acknowledged risks to children's health.

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[1] NRDC hereby moves for the affirmative relief of vacatur and remand pursuant to Federal Rule of Appellate Procedure 27(a)(3)(B). Counsel for EPA indicated that EPA would oppose NRDC's affirmative request.

BACKGROUND

The pesticide at issue in this appeal, tetrachlorvinphos ("TCVP"), is a dangerous chemical. It is a member of the organophosphate class of pesticides, which were developed from nerve warfare agents and can cause overstimulation of the nervous system leading to, among other things, vomiting and seizures. *See* Dkt. 16 at 10-11 ("NRDC Br."). Young children's exposure to TCVP is particularly troubling as, even at low levels, it may permanently harm their development. *See id.* at 12-15. EPA nonetheless has allowed TCVP to be used in the home—in the form of flea and tick shampoos and collars for pets—where children are exposed to it when they pet, play with, and even sleep with treated pets.

EPA has been cavalier in addressing the health risks posed to children by TCVP. *See id.* at 23-33. For years and years, EPA declined even to look at the exposure to children from flea collars. Meanwhile, NRDC studied the subject, found that TCVP pet products pose real risks to children, and in April 2009 petitioned EPA to cancel the registrations for these products based on scientific evidence pursuant to the Federal Insecticide, Fungicide, and Rodenticide Act ("FIFRA"). That statute prohibits EPA from registering a pesticide which causes

"unreasonable adverse effects on the environment," including human health. 7 U.S.C. §§ 136a(c)(5), 136(bb). And Congress specifically required EPA to "ensure" with "reasonable certainty that no harm will result to infants and children." 21 U.S.C. § 346a(b)(2)(C)(ii)(I).

Five years after filing its cancellation petition, having heard nothing in response, NRDC had to ask the U.S. Court of Appeals for the D.C. Circuit to issue a writ of mandamus directing EPA to respond to NRDC's petition. *See* Amended Petition for Writ of Mandamus, *In re NRDC*, No. 14-1017 (D.C. Cir. April 8, 2014). Only then did EPA finally act, denying NRDC's cancellation petition in November 2014. ER1-12.

In its decision denying NRDC's petition, EPA concluded that TCVP pet products do not pose any risks of concern. But EPA based this conclusion on a flawed risk assessment (the foundations of which EPA is no longer willing to defend). For example, among other flaws in the earlier risk assessment, EPA (1) abandoned a critical tenfold safety factor mandated by Congress to protect children (*see* NRDC Br. at 37-46); (2) completely ignored the only peer-reviewed, published study (the "Davis study") that directly measured people's exposure to TCVP from flea collars, despite the fact that NRDC had specifically raised this 2008

study in its cancellation petition (*see id.* at 52-60); and (3) analyzed children's exposure to TCVP from flea collars assuming the pesticide operated as a liquid, rather than a powder, even though the label on the flea collar box expressly states that the product works by producing a "fine white powder" (*see id.* at 66-70). Had EPA correctly accounted for any one of these errors, it would have concluded that the TCVP products pose unreasonable risks to children's health. *Id.* at 46, 60, 70.

NRDC promptly filed the instant petition for judicial review as a party adversely affected by EPA's decision, asking this Court to "review and set aside" EPA's decision pursuant to FIFRA § 16(b), 7 U.S.C. § 136n(b). Dkt. 1. In its opening brief, NRDC demonstrated that EPA's decision was unlawful and not supported by substantial evidence for the above (and other) reasons. And NRDC specifically asked the Court to vacate and remand EPA's decision. *See, e.g.*, NRDC Br. at 3, 71.

Shortly after NRDC filed its opening brief, EPA informed NRDC that it had reversed position on the children's tenfold safety factor and thus wanted to reconsider the denial order it had just issued nine months prior (which itself came five and a half years after NRDC filed its administrative petition). EPA accordingly moved for a voluntary

remand. Dkt. 22-1. Concerned about EPA's history of delay in these and similar FIFRA proceedings—and because the agency had not committed to fixing the other relevant flaws in its risk assessment—NRDC opposed EPA's motion. NRDC noted that because EPA's motion "relies only on what EPA 'intends' to do (but has not done yet)," denying the motion would not prejudice the agency because it could always renew its voluntary remand request with a "more concrete justification" after it "actually takes some of those intended steps." Dkt. 23-1 at 11.

The Court denied EPA's motion without prejudice, and allowed the agency to renew its motion within 60 days if it issued a new draft risk assessment during that time. Dkt. 25. EPA subsequently released a new draft risk assessment, as well as a memorandum responding to the main arguments NRDC raised in its opening brief. *See* Dkt. 26 at 5 & n.4 ("EPA Mot."). The draft risk assessment and accompanying memorandum undermine three basic foundations of EPA's earlier denial order—and do so largely based on information available to EPA at the time of its earlier decision—by (1) applying the tenfold children's safety factor; (2) acknowledging the relevance and prima facie validity of the peer-reviewed Davis study; and (3) conceding that the label on

the flea collar box indicates the product releases a powder.[2] The draft also acknowledges that applying these changes (or even some combination of them) results in risks above EPA's level of concern. In other words, EPA's new draft assessment now admits TCVP pet products may endanger children's health.

ARGUMENT

I. The Court Should Vacate EPA's Decision Before Remand.

A. This Is Not A Rare Circumstance Where Equity Demands Leaving A Challenged Decision In Force.

1. As a general rule, when this Court remands an agency decision for reconsideration, it will vacate the prior decision as well. The Court orders remand without vacatur "only in limited circumstances." *Pollinator Stewardship Council v. EPA,* 806 F.3d 520, 532 (9th Cir. 2015) (internal quotation marks omitted). Leaving the challenged decision in force during remand is appropriate solely "when equity demands." *Humane Soc'y v. Locke,* 626 F.3d 1040, 1053 n.7 (9th Cir. 2010) (quoting *Idaho Farm Bureau Fed'n v. Babbitt,* 58 F.3d 1392, 1405

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[2] *See, e.g.*, Wade Britton, EPA Memorandum, Tetrachlorvinphos (TCVP): Responses to Arguments Presented in the Natural Resources Defense Council, Inc.'s (NRDC) Aug. 5, 2015 Opening Brief in *NRDC v. EPA*, Case No. 15-70025 (9th Cir.) at 2-3, 6-8 (Dec. 21, 2015), *available at* http://tinyurl.com/hx2377h.

(9th Cir. 1995)). Such a remedy might be justified where, for example, vacatur would cause significant disruptive consequences, and yet the agency "may be able readily to cure" its prior action. *Id.* (internal quotation marks omitted). And "[w]hen deciding whether to vacate rulings by the EPA," in particular, this Court has generally only left EPA's challenged rulings in place where vacatur could "result in possible environmental harm." *Pollinator Stewardship Council,* 806 F.3d at 532; *see also Ctr. for Food Safety v. Vilsack,* 734 F. Supp. 2d 948, 951 (N.D. Cal. 2010) ("[T]he Ninth Circuit has only found remand without vacatur warranted by equity concerns in limited circumstances, namely serious irreparable environmental injury.").

Here, no equitable consideration supports—much less demands—leaving EPA's challenged decision in force on remand. Rather, the relevant considerations all validate the Court's presumptive remedy of vacatur and remand. Because "the government has not specifically requested that [the Court] remand without vacatur, and it is not otherwise apparent that the circumstances call for doing so," the "appropriate remedy" is to vacate EPA's decision and then remand to the agency. *Humane Soc'y,* 626 F.3d at 1053 n.7.

2. Vacating EPA's challenged decision in this case would cause no disruptive consequences nor pose any risk to the environment. The Court opted against vacatur in *California Communities Against Toxics v. EPA*, for example, based on the "severe" trouble that vacating EPA's decision would have created. 688 F.3d 989, 993-94 (9th Cir. 2012) (vacatur could lead to additional air pollution and regional blackouts and would be "economically disastrous" to a "billion-dollar venture employing 350 workers"); *see also Idaho Farm Bureau Fed'n*, 58 F.3d at 1405-06 (vacatur risked potential extinction of snail species); *W. Oil & Gas Ass'n v. EPA*, 633 F.2d 803, 813 (9th Cir. 1980) (vacatur would have unnecessarily thwarted operation of the Clean Air Act in California). Here, by contrast, vacating EPA's denial of NRDC's petition would result in no environmental harm or even, for that matter, any economic consequences to a third party because it would maintain the product registration that existed before EPA denied NRDC's petition.[3]

[3] This distinguishes the present case from *Ctr. for Food Safety v. EPA*, Case No. 14-73359, Dkt. 128 (9th Cir. Jan. 25, 2016), where the Court in a nonprecedential and unreasoned order remanded without vacating EPA's decision to register an herbicide under FIFRA. In that case, unlike here, the manufacturer of the herbicide intervened and opposed vacating the registration.

In fact, vacating EPA's decision before remanding—per this Court's usual practice—would be more protective of human health and the environment for at least two reasons. First, EPA sometimes relies on its prior denial orders as authority for its subsequent decisions on citizen petitions.[4] Thus, absent vacatur, EPA could rely on its earlier decision as a basis for denying other petitions to cancel the registration of dangerous pesticides—even though EPA now admits that the decision does not reflect its best scientific thinking, and did not account for relevant (and potentially dispositive) information that EPA had at its disposal when it made its earlier decision. And because EPA will not provide even an estimate for how long it will take to issue a new decision on remand, remand without vacatur could needlessly allow the prior decision to remain in force for a considerable amount of time.

Second, and relatedly, absent vacatur (or an order specifically requiring the agency to take action, *see infra* at 16-20), EPA may later

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[4] *See, e.g.*, Pyraclostrobin; Order Denying Objections to Issuance of Tolerances, 72 Fed. Reg. 52108, 52116 (Sept. 12, 2007) (citing EPA's prior denial order regarding other pesticides as authority for waiving the tenfold children's safety factor absent a required study); Order Denying Objections to Issuance of Tolerances, 70 Fed. Reg. 46706, 46716 (Aug. 10, 2005) (incorporating and relying on an earlier denial order in determining that the agency adequately assessed pesticide exposure to farmworkers' children and children in agricultural areas).

assert that it lacks any legal obligation to issue a revised response to NRDC's cancellation petition. That is, if the Court leaves EPA's earlier denial order in force, there will be no unanswered cancellation petition to which EPA must respond.[5] And unless EPA issues a new response to NRDC's cancellation petition on remand, the acknowledged health risks that TCVP pet products pose to children may never be resolved. Vacatur is therefore the correct remedy because leaving the prior decision in place "risks more potential environmental harm than vacating it." *Pollinator Stewardship Council,* 806 F.3d at 532.

3. Vacatur is also appropriate here because EPA acknowledges that "on remand, a different result may be reached." *Id.* EPA's draft risk assessment admits that—accounting for the tenfold children's safety factor, the Davis study, and the product formulation identified on the flea collar box (i.e., the major arguments NRDC raised in this appeal)—TCVP pet products may endanger children's health. EPA's own actions therefore support vacatur because they express "significant doubts as to whether the agency chose correctly." *Am. Petroleum Inst.*

[5] EPA's motion notably makes no binding commitment that the agency will, in fact, issue a revised response; it represents only that EPA presently *intends* to do so. *See* EPA Mot. at 2, 5, 8 & n.7, 10.

v. Johnson, 541 F. Supp. 2d 165, 185 (D.D.C. 2008) (internal quotation marks omitted). And even if EPA again denies NRDC's cancellation petition—which it lawfully should not—it will do so only after completely rewriting major parts of its underlying risk assessment. "In light of the need for wholesale revision" of the basis of EPA's prior decision, the "appropriate course is to vacate" that decision before remanding. *NRDC v. EPA*, 489 F.3d 1250, 1262 (D.C. Cir. 2007).

In sum, vacatur would result in no disruptive consequences and would prevent EPA's prior decision—which may be reversed and cannot "survive[] remand in anything approaching recognizable form," *id.* at 1261—from being used as potentially harmful precedent on remand.

B. EPA's Decision Should Be Vacated As A Matter Of Fairness Because Remand Without Vacatur Would Not Provide The Remedy That NRDC Sought.

1. NRDC brought this petition for judicial review pursuant to its statutory right under FIFRA § 16(b), which provides: "Upon the filing of such petition the court shall have exclusive jurisdiction to affirm or set aside the order complained of in whole or in part." 7 U.S.C. § 136n(b). This provision makes clear that the Court presently has authority to vacate—or "set aside"—EPA's decision denying NRDC's cancellation

petition. And the Court's authority is not constrained by the fact that EPA requested a voluntary remand before NRDC received the independent adjudication of the merits that it sought. That is, although "the Court does not actually rule on the merits" when it grants an agency's voluntary remand motion, "the same equitable analysis for vacatur of the rules during remand should apply." *NRDC v. U.S. Dep't of Interior,* 275 F. Supp. 2d 1136, 1143 (C.D. Cal. 2002).[6]

2. Consistent with § 16(b), NRDC specifically petitioned this Court to review "and set aside" EPA's decision denying NRDC's cancellation petition. Dkt. 1-2. And NRDC's opening brief made its desire for vacatur perfectly clear, repeating this request no fewer than four separate times. *See* NRDC Br. at 3, 8, 45, 71. EPA's motion is

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[6] *See also, e.g., Ctr. for Native Ecosystems v. Salazar*, 795 F. Supp. 2d 1236, 1241-42 (D. Colo. 2011) ("vacation of an agency action without an express determination on the merits is well within the bounds of traditional equity jurisdiction"); *Coal. of Ariz./N.M. Ctys. for Stable Econ. Growth v. Salazar*, No. 07-CV-00876 JEC/WPL, 2009 WL 8691098, at *3 (D.N.M. May 4, 2009) (same). Although some district courts have concluded in the Administrative Procedure Act ("APA") context that they cannot vacate an agency's decision without first adjudicating the merits, their logic turned on factors specific to the APA and thus, whatever force those cases may have, they do not extend to the FIFRA § 16(b) petition at issue here. *See, e.g., Carpenters Indus. Council v. Salazar*, 734 F. Supp. 2d 126, 135-36 (D.D.C. 2010) (noting that the APA judicial review provision, 5 U.S.C. § 706(2), refers to the court setting aside agency actions "found to be" unlawful).

therefore disingenuous when it presents the half-truth that "remand is the ultimate outcome that NRDC seeks in this litigation." EPA Mot. at 9. Because NRDC expressly requested *vacatur and* remand, not just remand, a ruling that leaves EPA's decision in force on remand plainly would not provide the outcome that NRDC sought.

And it would be unfair to let EPA preempt that remedy simply because it moved for voluntary remand before the Court heard NRDC's arguments on the merits. If an agency is unwilling to defend its prior decision, then it should not also be allowed to leave that decision in force. Such an outcome would be unfairly prejudicial to petitioners, like NRDC here, who exercise their right to challenge an agency decision yet are denied the opportunity to press their arguments before the Court.

3. A similar fairness principle has long governed the remedy in the analogous situation where, for reasons outside an appellant's control, a civil suit becomes moot on appeal. In that situation, the "'established' (though not exceptionless)" practice is to "vacate the judgment below," despite the fact that the appellate court cannot review the merits. *Camreta v. Greene*, 131 S. Ct. 2020, 2035 (2011) (citing *United States v. Munsingwear, Inc.*, 340 U.S. 36, 39 (1950)); *accord Log*

Cabin Republicans v. United States, 658 F.3d 1162, 1167-68 (9th Cir. 2011) (per curiam). "A party who seeks review of the merits of an adverse ruling, but is frustrated by the vagaries of circumstance, ought not in fairness be forced to acquiesce in" that decision. *U.S. Bancorp Mortg. Co. v. Bonner Mall P'ship*, 513 U.S. 18, 25 (1994). Vacating the challenged decision in such situations ensures a just outcome for "those who have been prevented from obtaining the review to which they are entitled." *Munsingwear*, 340 U.S. at 39.

There is no reason to treat an agency's voluntary remand any differently. In a voluntary remand, no less than a civil case mooted on appeal, vacatur must remain the default remedy because, otherwise, "leaving the [challenged decision] in place during remand would ignore petitioners' potentially meritorious challenges." *NRDC*, 489 F.3d at 1262 (internal quotation marks omitted). Here, NRDC sought review of the merits of EPA's denial order, filed its opening brief, and requested specifically that the decision be vacated pursuant to §16(b). But if the Court accedes to EPA's voluntary remand request, NRDC—for reasons outside its control—will be precluded from obtaining judicial review of that decision (and, possibly, from obtaining any judicial review

whatsoever, *see infra* at 19). Vacatur is therefore appropriate to "strip[] the decision below of its binding effect" and prevent EPA's challenged (but unreviewed) decision from "spawning any legal consequences." *Camreta*, 131 S.Ct. at 2035 (internal quotation marks omitted).

II. At The Very Least, The Court Should Impose A Deadline For EPA To Issue A Revised Response On Remand.

1. In addition, and at a minimum, the Court should impose a deadline on the remand to ensure that EPA promptly revises its response to NRDC's petition and addresses the acknowledged risks to children's health. Both voluntary remands and remands without vacatur raise concerns about agency delay because neither provides an incentive for the agency to act in a timely manner. *See* Toni M. Fine, *Agency Requests for "Voluntary" Remand*, 28 Ariz. St. L.J. 1079, 1096 n.70 (1996) (noting that an agency may "react to a remand ordered at its own request with less of a sense of responsibility to act quickly than it would on remand at the court's direction"); Kristina Daugirdas, Note, *Evaluating Remand Without Vacatur*, 80 N.Y.U. L. Rev. 278, 300 (2005) (analyzing "agencies' disincentives to act in response" to a remand without vacatur). And instances of multi-year delays following such remedies have led some judges to "urge future panels to consider the

alternatives," like imposing deadlines on the agency during remand. *In re Core Commc'ns, Inc.*, 531 F.3d 849, 862 (D.C. Cir. 2008) (Griffith, J., concurring). Indeed, courts have imposed such deadlines accompanying both voluntary remands[7] and remands without vacatur.[8]

2. Imposing a deadline is particularly important in this case, given the acknowledged health risks to children and EPA's history of delay in these and similar FIFRA proceedings. As explained above, EPA waited five and a half years—and only after NRDC resorted to seeking mandamus—before even responding to NRDC's administrative petition. And the lengthy delay in this case was not an isolated incident. After eight years of broken promises by the agency, this Court recently granted NRDC's mandamus petition—and imposed a deadline on EPA—in a similar FIFRA proceeding regarding another

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[7] *See* Fine, 28 Ariz. St. L.J. at 1087, 1126-30; *see also, e.g., Greater Yellowstone Coal. v. EPA*, No. 4:12-CV-60-BLW, 2013 WL 1760286, at *3 (D. Idaho Apr. 24, 2013) (requiring EPA to act within 90 days and "maintain[ing] jurisdiction to ensure a timely remand process"); *NRDC*, 275 F. Supp. 2d at 1141-43 (ordering the agency to complete its remanded proceedings within ten months, and retaining jurisdiction).

[8] *See* Daugirdas, 80 N.Y.U. L. Rev. at 301-05; *see also, e.g., Nat'l Ass'n of Regulatory Util. Comm'rs v. DOE*, 680 F.3d 819, 826 (D.C. Cir. 2012) (ordering agency to "respond to the remand within six months" and retaining jurisdiction); *A.L. Pharma, Inc. v. Shalala*, 62 F.3d 1484, 1492 (D.C. Cir. 1995) (ordering the rule "vacated automatically" absent adequate justification from the agency within 90 days).

organophosphate pesticide, chlorpyrifos. *See In re Pesticide Action Network N. Am.* ("*PANNA*"), 798 F.3d 809 (9th Cir. 2015).

As in that case, EPA's request for an open-ended remand here does not provide a "'concrete timeline' for resolving [NRDC's] petition," but rather merely "a roadmap for further delay." *Id.* at 814. EPA asserts in its present motion that it "*intends* to conclude reconsideration of NRDC's petition within a reasonable period of time," EPA Mot. at 10 (emphasis added), but it nowhere *commits* to doing so—nor does it even provide an estimate for how long that may be. EPA's present intentions provide little comfort given the agency's "significant history of missing the deadlines it has set." *PANNA*, 798 F.3d at 814. And they carry even less weight in this, an election year, as they do not account for a potential change in administration: Absent vacatur or a deadline imposed by this Court, EPA under a new administrator might assert that it lacks a legal obligation even to issue a revised response to NRDC's petition, much less to issue one in a timely manner.

3. Accordingly, this Court should—at a minimum—order that EPA issue a revised response to NRDC's cancellation petition by the end of 2016, and the Court should retain jurisdiction to enforce that

deadline. This deadline would give the agency more than six months to finalize its risk assessment after the public comment period closes on its current draft[9], and then another 90 days to issue its revised response to NRDC's petition (as is EPA's current intention, *see* EPA Mot. at 10).

EPA apparently opposes a court-ordered deadline and suggests that NRDC should instead request the extraordinary relief of mandamus to address any delay that results on remand. *See id.* at 9 n.8. But unless this Court vacates EPA's earlier decision or orders the agency to issue a revised response, it is not even clear that NRDC would have a basis on which to seek mandamus, since EPA may later disclaim any legal obligation to act. Granting EPA's request for an open-ended remand could therefore deprive NRDC—and this Court—of *any* opportunity for judicial review altogether. Moreover, courts have relied on an agency's "disposition to delay" as a reason to impose a deadline and retain jurisdiction on remand "so that any further review would be

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[9] EPA maintains that it cannot yet determine how long it will take to finalize its risk assessment, but promises it will be able to provide such an estimate "within 45 days of the close of the comment period" on the present draft. EPA Mot. at 10. Thus, if the Court is reluctant to impose a deadline on EPA before giving the agency an opportunity to provide that estimate, it should hold this case in abeyance and order EPA to provide a status report 45 days after the comment period closes, so that the Court may impose an appropriate deadline at that time.

expedited." *Nat'l Ass'n of Regulatory Util. Comm'rs v. DOE*, 680 F.3d 819, 820, 826 (D.C. Cir. 2012). And EPA's sluggish disposition has already forced NRDC to resort to mandamus once in this case and twice in the chlorpyrifos litigation. *See PANNA*, 798 F.3d at 812.

Given this history, and the way this appeal has proceeded, it should therefore be EPA's burden to request a deadline extension and justify any further delays that occur on remand—rather than NRDC's burden to justify the extraordinary remedy of mandamus. After all, because EPA is the party that is no longer willing to defend its prior decision, it should bear the burden of explaining why that decision should remain in force—and these dangerous products should remain on the shelves, and in children's homes—any longer than necessary.

CONCLUSION

For the foregoing reasons, the Court should vacate EPA's denial order before remanding. In addition, and at a minimum, the Court should impose a deadline for EPA to issue a revised response to NRDC's administrative petition on remand.

Dated: February 25, 2016 Respectfully submitted,

/s/ Susannah Landes Weaver

Susannah Landes Weaver
Ian Fein
Kelsi Brown Corkran
ORRICK, HERRINGTON & SUTCLIFFE LLP
1152 15th Street, NW
Washington, DC 20005
Telephone: (202) 339-8400
sweaver@orrick.com

Mae Wu
NATURAL RESOURCES DEFENSE COUNCIL
1152 15th Street, NW, Suite 300
Washington, DC 20005
Telephone: (202) 289-6868
mwu@nrdc.org

Counsel for Petitioner

Exhibit N

No. 15-70025

UNITED STATES COURT OF APPEALS
FOR THE NINTH CIRCUIT

NATURAL RESOURCES DEFENSE COUNCIL, INC.,

Petitioner,

v.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY,

Respondent.

REPLY IN SUPPORT OF RESPONDENT'S RENEWED MOTION FOR VOLUNTARY REMAND AND OPPOSITION TO PETITIONER'S MOTION FOR VACATUR

Petitioner Natural Resources Defense Council ("NRDC") does not oppose Respondent United States Environmental Protection Agency's ("EPA" or "Agency") Renewed Motion for Voluntary Remand. *See* NRDC's Resp. to Renewed Mot. for Voluntary Remand & Request for Vacatur at 1 (Feb. 25, 2016) [Dkt. 27] (hereinafter "NRDC Mot."). Thus, the parties are in agreement that this Court should remand EPA's decision concerning NRDC's administrative petition to cancel the registered pet uses of the pesticide tetrachlorvinphos ("Response to the Cancellation Petition"). Remand is the most efficient and logical way for this case to proceed. It will save this Court's time and resources and enable the

Agency to focus on completing its new risk assessment for tetrachlorvinphos and on reevaluating its decision in view of that new risk assessment, which could moot or significantly narrow the issues raised by NRDC in this litigation.

NRDC's Motion for Vacatur should be denied, however. EPA's Response to the Cancellation Petition was a reasonable exercise of the Agency's technical expertise based on the record available at the time. EPA confesses no error in that decision. EPA is committed to assessing the impact of new scientific developments on its prior decision and, in the interests of saving judicial and agency resources, moved for remand before the completion of briefing in this case. It would be premature and prejudicial to EPA for this Court effectively to rule on the merits of NRDC's petition for review without full briefing. Moreover, vacating the decision during the remand proceedings will not benefit the public, because tetrachlorvinphos pet products can continue to be legally sold. Finally, NRDC would not be prejudiced by remand without vacatur. Thus, vacatur is not justified in this case.

In the event that this Court wishes to retain jurisdiction pending further administrative developments, EPA requests in the alternative that this case be held in abeyance while the Agency evaluates public comments received on the draft risk assessment for tetrachlorvinphos and that the Court consider EPA's and NRDC's Motions after that process is complete.

ARGUMENT

I. This Court Should Remand EPA's Decision Without Vacatur.

A. Granting Vacatur Would Be Premature.

It would be premature for this Court to vacate EPA's Response to the Cancellation Petition because the parties have not completed briefing and all relevant excerpts of the Agency's administrative record are not before the Court. The very standard this Court uses to evaluate vacatur—balancing the seriousness of deficiencies in the administrative action against the disruptive consequences of immediate vacatur—presupposes that the Court finds the agency action to be deficient. *See, e.g., Cal. Cmtys. Against Toxics v. EPA*, 688 F.3d 989, 992 (9th Cir. 2012) ("Whether agency action should be vacated depends on how serious the agency's errors are 'and the disruptive consequences of an interim change that may itself be changed.'") (citation omitted). Because this Court does not have all of the information necessary to make a determination on the merits of EPA's Response to the Cancellation Petition—nor should it consume unnecessary resources making such a determination, for all of the reasons stated in EPA's Renewed Motion for Voluntary Remand—vacatur would not be appropriate.[1]

[1] NRDC claims that EPA's shift in scientific understanding automatically renders the Agency's prior decision deficient. *E.g.*, NRDC Mot. at 10. Until EPA finalizes the new risk assessment for tetrachlorvinphos and completes its
(footnote continued...)

Where voluntary remand is sought before full briefing, courts have declined to vacate agency actions. *See, e.g., Ctr. for Food Safety v. EPA*, No. 14-73359, Dkt. 128, Order (9th Cir. Jan. 25, 2016) ("Enlist Duo Order"); *Am. Forest Res. Council v. Ashe*, 946 F. Supp. 2d 1, 42 (D.D.C. 2013) (granting agency's motion for voluntary remand but declining to vacate decision because "it would be premature to decide the merits" before full briefing and filing of administrative record, especially when agency did not request vacatur), *aff'd*, 601 Fed. Appx. 1 (D.C. Cir. 2015); *Nat'l Parks Conservation Ass'n v. Salazar*, 660 F. Supp. 2d 3, 4 (D.D.C. 2009) (declining to vacate rule and distinguishing cases vacating agency actions on the grounds that the courts first decided the actions were unlawful on the merits).

NRDC dismisses this Court's order in *Center for Food Safety* as "unreasoned," NRDC Mot. at 9 n.3, but it is noteworthy (even if not precedential) that the Court declined to vacate the registration for the pesticide product Enlist

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reconsideration of NRDC's petition for cancellation, no one can predict what the ultimate outcome of reconsideration will be. Even if this Court were to agree with NRDC, vacatur would still not be required. *See, e.g., Pacific Bell v. Pac-West Telecomm, Inc.*, 325 F.3d 1114, 1122-23 (9th Cir. 2003) (holding that agency actions can remain in place pending completion of remand even after being found arbitrary and capricious); *Cal. Cmtys. Against Toxics*, 688 F.3d at 992 ("A flawed rule need not be vacated."); *A.L. Pharma, Inc. v. Shalala*, 62 F.3d 1484, 1492 (D.C. Cir. 1995) (holding that a court has discretion to remand agency decision without vacatur where the court believes the agency could sufficiently explain the decision on remand).

Duo *even after EPA had requested vacatur*. *See* Enlist Duo Order at 2. This Court concluded that the issue could be addressed administratively, stating that "[t]he motion for voluntary vacatur of the registration of Enlist Duo is denied without prejudice to the rights of either party to litigate that question before the agency." *Id.* As in this case, briefing was not completed in *Center for Food Safety* when the Court remanded the pesticide registration without vacatur. Moreover, EPA opposes vacatur here.

Although NRDC cites three district court cases for the proposition that this Court may entertain vacatur even though briefing is not yet complete, none of those cases actually resulted in vacatur of the challenged agency action. *See* NRDC Mot. at 13 & n.6 (citing *NRDC v. U.S. Dep't of Interior*, 275 F. Supp. 2d 1136 (C.D. Cal. 2002); *Ctr. for Native Ecosystems v. Salazar*, 795 F. Supp. 2d 1236 (D. Colo. 2011); *Coal. of Ariz./N.M. Ctys. for Stable Econ. Growth v. Salazar*, No. 07-cv-00876 JEC/WPL, 2009 WL 8691098, at *3 (D.N.M. May 4, 2009)). Moreover, NRDC cites no precedent where this Court vacated agency action at this stage of the proceedings, let alone over the agency's objections.

Thus, this Court need not—and should not—prematurely decide the legality of EPA's Response to the Cancellation Petition based on a single brief and limited

excerpts of the record.[2] To do so would only undermine one of the key goals of remand—saving judicial time and resources.

B. The Balance of Equities Weighs Against Vacatur.

Even if this Court were inclined to consider NRDC's arguments for vacatur at this time, on balance, the equities weigh against vacatur. *See Idaho Farm Bureau Fed'n v. Babbitt*, 58 F.3d 1392, 1405-06 (9th Cir. 1995) (weighing the equities of vacating agency action) (citation omitted).

1. Vacatur Would Unduly Prejudice EPA Because Agencies Can Reconsider Their Decisions Without Confessing Error.

First, vacating a decision that EPA wants to reconsider in light of evolving science—and not because it was unsupported at the time—would be unduly prejudicial to EPA and would depart from well-established precedent that an administrative agency has the inherent authority to reconsider its decisions *without* confessing error. *See SKF USA Inc. v. United States*, 254 F.3d 1022, 1029 (Fed. Cir. 2001). EPA confesses no error here. The November 6, 2014 Response to the Cancellation Petition was a reasonable exercise of EPA's technical expertise and supported by a risk assessment conducted solely in response to NRDC's petition.

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[2] EPA also cautions that some of the materials cited in NRDC's opening brief may not even be part of the administrative record. *See* NRDC's Br., Table of Auths. vii-viii [Dkt. 16] (including 18 "Other Authorities" that are not listed on the Agency's Certified Index to the Administrative Record [Dkt. 6]).

See EPA's Renewed Mot. for Voluntary Remand 4 (Feb. 11, 2016) [Dkt. 26] (hereinafter "EPA Renewed Mot."). Thus, contrary to NRDC's insinuation, EPA is not "unwilling to defend its prior decision." *See* NRDC Mot. at 14. Rather, proceeding with full merits briefing and argument is simply no longer the most logical or efficient use of this Court's or the Agency's time.

EPA is seeking remand because of a recent shift in scientific thinking concerning tetrachlorvinphos and other organophosphate pesticides. *See* EPA Renewed Mot. at 4-6. The Agency's scientific understanding and proceedings on remand will be informed by public comments received on the December 2015 Draft Human Health Risk Assessment for Tetrachlorvinphos ("Draft Risk Assessment"). *See* 81 Fed. Reg. 3128 (Jan. 20, 2016)). And the new risk assessment for tetrachlorvinphos is being conducted as part of the independent registration review process required by the statute governing pesticides, the Federal Insecticide, Fungicide, and Rodenticide Act ("FIFRA"). EPA Renewed Mot. at 3-4.

Vacating EPA's prior decision in this case could deter agencies from voluntarily reconsidering their actions under these or other circumstances. *See SKF USA Inc.*, 254 F.3d at 1028-30 (discussing many reasons why an agency could seek to voluntarily reconsider its decision, such as to consider new information or simply to reconsider the decision's "correctness").

2. NRDC Will Not Be Prejudiced if EPA's Decision Remains Intact During Remand Proceedings.

NRDC will not be unduly prejudiced if this Court denies its Motion for Vacatur. At the end of reconsideration, EPA will issue a new response to NRDC's petition for cancellation. Whether that response will be a grant, denial, or partial grant and partial denial of the petition based on application of the new risk assessment for tetrachlorvinphos is speculative at this time. But regardless of the outcome, NRDC will be in the same position at that time whether or not this Court has vacated EPA's prior decision following full briefing and a merits determination.

NRDC claims that it would not be "fair" to deprive NRDC of vacatur when that is a remedy it seeks. NRDC Mot. at 12-14. The fact that NRDC requested vacatur is not a justification for vacatur. Under this strained logic, EPA's opposition to vacatur would weigh against vacatur, effectively canceling out NRDC's request anyway. NRDC's attempt to equate voluntary agency remand with this Court vacating a district court's judgment if the case becomes moot on appeal is also unpersuasive. *See id.* at 14. Federal courts are bound by the Constitution to evaluate whether they have jurisdiction over active cases or controversies before deciding cases on the merits. *E.g.*, *Maldonado v. Lynch*, 786 F.3d 1155, 1160 (9th Cir. 2015) ("When there are developments in a proceeding

that suggest that it may be moot, we have an obligation to inquire whether a case or controversy under Article III of the Constitution continues to exist.") (citations omitted). No such limitation is placed on this Court's discretion to leave an agency action intact when the agency seeks voluntarily remand without vacatur.

Lastly, NRDC's assertion that it could be prejudiced if the Response to the Cancellation Petition is not vacated before a change in administration is unjustified and purely speculative. *See* NRDC Mot. at 18 ("Absent vacatur . . . , EPA under a new administration might assert that it lacks a legal obligation even to issue a revised response to NRDC's petition, much less to issue one in a timely manner."). NRDC cites no authority in which a court vacated agency action on such a speculative basis. And, as noted above, vacating EPA's decision would not guarantee any particular outcome at the end of the remand proceedings because EPA must still evaluate NRDC's petition in light of the new risk assessment for tetrachlorvinphos.

3. Leaving EPA's Decision Intact During Remand Would Not Harm Human Health or the Environment.

Leaving EPA's prior decision intact during remand would cause no harm to human health or the environment. *See A.L. Pharma, Inc. v. Shalala*, 62 F.3d 1484, 1492 (D.C. Cir. 1995) (holding that remand without vacatur is appropriate where no significant harm would result from allowing the decision to remain in effect);

Fox Television Stations, Inc. v. FCC, 280 F.3d 1027, 1048-49 (D.C. Cir. 2002) (noting that vacatur is not "necessarily indicated" even if "disruptive consequences of vacatur might not be great"), *modified on other grounds*, 293 F.3d 537 (D.C. Cir. 2002). *See also Nat'l Wildlife Fed'n v. Espy*, 45 F.3d 1337, 1343 (9th Cir. 1995) (noting that courts "must weigh 'the competing claims of injury . . . and the effect on each party of the granting or withholding of the requested relief.'") (quoting *Amoco Prod. Co. v. Village of Gambell*, 480 U.S. 531, 542 (1987)).

In fact, leaving the Response to the Cancellation Petition intact while EPA completes remand is just as protective of human health and the environment as vacating the decision. Regardless of whether this Court vacates the Response to the Cancellation Petition, tetrachlorvinphos pet products can be legally sold under the existing FIFRA registrations.

NRDC's arguments that vacatur would be more protective of human health and the environment are unfounded. First, NRDC claims that "remand without vacatur could needlessly allow the prior decision to remain in force for a considerable amount of time." NRDC Mot. at 10. But the prior decision not to cancel pet uses of tetrachlorvinphos did not change the legal status of that pesticide. Neither would vacatur of that decision. Whether EPA's decision remains intact during or is vacated before remand proceedings has no bearing on human health or the environment. The status quo—the legal sale of registered

tetrachlorvinphos pet products—is maintained either way. And EPA is committed to completing remand proceedings in a reasonable time frame. Second, NRDC's claim that EPA would rely on the Response to the Cancellation Petition "as a basis for denying other petitions" to cancel registrations is not only speculative but also presumes—without cause—that the Agency would rely on a decision while actively reconsidering it. *See id.* at 10 & n.4.

C. This Court Should Not Impose a Schedule on Remand.

NRDC's request that this Court "at a minimum" impose a deadline on EPA's remand proceedings is also unfounded and should be denied. *See* NRDC Mot. at 16-20.

As an initial matter, the applicable judicial review provision in FIFRA limits this Court's authority to "affirm or set aside" an agency order based on whether such order is "supported by substantial evidence when considered on the record as a whole." 7 U.S.C. § 136n(b). Nothing in this provision expressly provides the Court with authority to impose the deadline sought by NRDC on remand, much less before EPA has even filed its brief on the merits. And NRDC cites no other authority in its Motion that supports NRDC's position that this Court could and

should condition remand in this case. Rather, NRDC principally relies on law review articles and dicta in a concurring opinion. NRDC Mot. at 16-17.[3]

Even if this Court could grant the relief sought by NRDC, there is no practical or factual basis on which the Court should do so. EPA already presented to the Court in its Renewed Motion a reasonable plan for a further proceeding on remand. The public comment period on the Draft Risk Assessment is currently open. *See* 81 Fed. Reg. at 3128 (stating that comments on the Draft Risk Assessment will be accepted until March 21, 2016). Once EPA considers public comments received, the Agency will finalize the risk assessment. *See* EPA Renewed Mot. at 5. EPA plans to revise its response to NRDC's petition within 90

[3] None of the cases cited in footnotes 7-8 of NRDC's Motion concerned FIFRA or involved the kind of scientific analyses EPA needs to conduct here. In *Greater Yellowstone Coalition v. EPA*, for example, the court ordered EPA to conclude its voluntary remand proceedings on a narrow Clean Water Act matter within 90 days *where EPA proposed and the parties agreed* that 90 days was a reasonable amount of time to complete remand. Case No. 4:12-cv-60-BLW, 2013 WL 1760286, at *2-3 (D. Idaho Apr. 24, 2013). In *National Association of Regulatory Utility Commissioners v. Department of Energy*, the court held that the Department of Energy failed for several years to comply with a statutory mandate to reassess annually fees being charged to generators of nuclear waste even after the circumstances necessitating the fees changed, and gave the agency six months to do so on remand. 680 F.3d 819, 820-26 (D.C. Cir. 2012). The court reasoned that it was not appropriate to suspend the fees and, thus, setting a deadline would ensure that the agency acted expeditiously on remand. *Id.* at 820. Finally, in *A.L. Pharma, Inc. v. Shalala*, the court gave the Food and Drug Administration 90 days to provide additional justification for what the court deemed an invalid decision to approve a drug rather than vacating the decision outright. 62 F.3d at 1492.

days after finalizing the risk assessment. *Id.* NRDC does not contest these aspects of EPA's plan. NRDC nonetheless asks this Court to order EPA to complete remand proceedings by the end of 2016. NRDC Mot. at 18-19.

As explained in EPA's Renewed Motion for Voluntary Remand, the amount of time the Agency needs to consider and respond to public comments is entirely dependent on the number and complexity of comments received. EPA Renewed Mot. at 10. Until it has an opportunity to review the public comments on the Draft Risk Assessment, EPA is not in a position to determine how long the Agency will need to finalize the risk assessment. As stated in EPA's opening motion, the Agency will be able to provide an estimate as to how much time it will take to complete the final risk assessment within 45 days after the close of the comment period. *Id.*

Since EPA is unable at this time to determine how long the Agency will need to finalize the risk assessment for tetrachlorvinphos, it is not surprising that NRDC itself does not attempt to explain why its proposed deadline of "the end of 2016" is reasonable. Rather, NRDC's proposal appears to be motivated by a desire for EPA to complete remand proceedings before the change in administration following the November 2016 presidential election. *See* NRDC Mot. at 18-19. NRDC cites no authority that would enable this Court to impose a deadline for remand based on a potential political change. And confining remand on this basis

or otherwise imposing an arbitrary deadline for EPA to finalize the risk assessment, without knowing the depth and volume of public comments, could undermine any cancellation proceedings that might ultimately flow from the final risk assessment.

Before any tetrachlorvinphos registrations could be cancelled, EPA must submit a draft notice of intent to cancel that incorporates the final risk assessment to a Science Advisory Panel, among others, in order to obtain the Panel's advice on the scientific bases for cancellation. *See* 7 U.S.C. §§ 136w(d)(1), 136d(b). The Panel holds a public meeting on the science issues involved in potential cancellation and thereafter issues its comments. EPA must publish the Panel's comments and the Agency's response to those comments. *Id.* The Agency may then publish a final notice setting forth its bases for cancellation and provide affected registrants and other interested persons with an opportunity for a formal adjudicatory hearing on the proposed cancellation before an Administrative Law Judge. *See* 7 U.S.C. § 136d(b); 40 C.F.R. §§ 164.21, 164.23. If the Panel or the Administrative Law Judge has any reservations about the scientific basis for cancellation, or if EPA significantly revises its scientific position after the cancellation process has begun, EPA's ability to successfully prosecute a cancellation action (and to do so in a timely manner) could be severely hampered. Thus, it is crucial that EPA be allowed to undertake a comprehensive consideration

of and response to comments raising legitimate scientific issues before finalizing its risk assessment and possibly initiating any cancellation action.

In short, NRDC's request amounts to asking this Court to anticipate what would be an unreasonable delay before the public comment period closes, and ignores the well-established principle that mandamus, not a schedule on remand, is the appropriate relief if there were such a delay.[4] *See, e.g., NRDC v. EPA*, 489 F.3d 1364, 1375 (D.C. Cir. 2007).

Accordingly, EPA requests that the Court remand the Response to the Cancellation Petition to the Agency for further consideration—without vacatur and without a deadline. If, however, this Court is not inclined to grant the relief requested by EPA, EPA does not oppose a continuation of abeyance until the Agency has time to evaluate the public comments received in the draft risk

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[4] NRDC once again conflates this case with the mandamus case *Pesticide Action Network North America v. EPA*, 798 F.3d 809 (9th Cir. 2015) ("*PANNA*"). *See* NRDC Mot. at 17-18. In *PANNA*, this Court granted a renewed petition for writ of mandamus to compel EPA to act on a 2007 administrative petition to revoke the tolerances for a different pesticide, chlorpyrifos. 798 F.3d at 815. This case is not about mandamus or chlorpyrifos. In contrast to *PANNA*, EPA has acted here; its November 2014 decision concerning NRDC's petition to cancel the pet uses of tetrachlorvinphos is the subject of this case. And *PANNA* has no bearing on whether EPA will complete remand proceedings in this case in a reasonable time frame; the Agency has already completed the first milestone of its plan for remand in a timely manner by issuing the Draft Risk Assessment in December 2015. NRDC's attempts to blur the clear distinctions between *PANNA* and this case should be rejected.

assessment for tetrachlorvinphos. *See* NRDC Mot. at 19 n.9 (proposing continuation of abeyance for this period of time). As stated above, EPA will be able to provide an estimate as to how much time it will take to complete the final risk assessment within 45 days of the close of the comment period and could submit a status report at that time.

CONCLUSION

For the foregoing reasons, EPA respectfully requests that the Court remand the Response to the Cancellation Petition to the Agency for further consideration—without vacatur and without a deadline.

Dated: March 10, 2016

Respectfully submitted,

JOHN C. CRUDEN
Assistant Attorney General
Environment & Natural Resources Division

s/ *Erica M. Zilioli*
ERICA M. ZILIOLI
U.S. Department of Justice
Environmental Defense Section
P.O. Box 7611
Washington, DC 20044
Telephone: (202) 514-6390
Facsimile: (202) 514-8865
Erica.Zilioli@usdoj.gov

Of Counsel:

BENJAMIN WAKEFIELD
Office of General Counsel
U.S. Environmental Protection Agency
William Jefferson Clinton Building North
1200 Pennsylvania Avenue, N.W.
Washington, DC 20460

Exhibit O

UNITED STATES COURT OF APPEALS

FOR THE NINTH CIRCUIT

NATURAL RESOURCES DEFENSE COUNCIL, INC., Petitioner, v. U.S. ENVIRONMENTAL PROTECTION AGENCY, Respondent.	No. 15-70025 ORDER

Before: O'SCANNLAIN, CLIFTON, and WATFORD, Circuit Judges.

Respondent's motion for remand (Docket Entry No. 26) is granted.

Petitioner's motion for vacatur (Docket Entry No. 27) is denied.

REMANDED.

AT/MOATT

Exhibit P

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

MEMORANDUM

Date: December 21, 2016

SUBJECT: **Tetrachlorvinphos (TCVP)** Revised Human Health Risk Assessment for Registration Review

PC Code: 083701, 083702
Petition No.: NA
Risk Assessment Type: Single Chemical Aggregate
TXR No.: NA
MRID No.: NA

DP Barcode: 436834
Registration Nos.: NA
Regulatory Action: Registration Review
Case No.: 1321
CAS No.: 22248-79-9
40 CFR: §180.252

FROM: Danette Drew, Chemist
Linda Taylor, Ph.D. Toxicologist
Kelly Lowe, Environmental Scientist
Risk Assessment Branch V/VII
Health Effects Division (HED, 7509P)

And

Wade Britton, MPH, Environmental Health Scientist
Risk Assessment Branch IV
Health Effects Division (HED, 7509P)

THROUGH: Michael Metzger, Branch Chief
Risk Assessment Branch V/VII
Health Effects Division (HED, 7509P)

TO: James Parker, Chemical Review Manager
Neil Anderson, Branch Chief
Risk Management and Implementation Branch I
Pesticide Re-evaluation Division (7508P)

Attached is HED's revised human health risk assessment in support of the registration review of the insecticide tetrachlorvinphos (TCVP).

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1.0 Executive Summary

The insecticide tetrachlorvinphos (TCVP) [(Z)-2-chloro-1-(2,4,5-trichlorophenyl) vinyl dimethyl phosphate] is a member of the organophosphate (OP) class of pesticides. TCVP is used as a dermal or oral treatment to livestock (i.e., cattle, swine, poultry and horses) and their premises, in kennels, outdoors as a perimeter treatment, and as a flea treatment on cats and dogs. Formulations for pet use include collars, dusts/powders, and pump and trigger sprays. The other (non-pet) uses include dusts (D), emulsifiable concentrates (EC), feed through (solid and liquid food additives), feed blocks, and wettable powders (WP). Human exposure to TCVP in food may occur as a result of consuming residues in animal commodities (e.g., meat). Exposure may also occur from drinking water that may contain TCVP residues as a result of some outdoor use patterns. Residential exposures may occur as a result of applying flea products to pets (cats and dogs) or contacting treated pets. Occupational exposures may occur during application of TCVP to livestock or their premises, or during outdoor perimeter or kennel treatments. Occupational exposures may also occur to veterinarians and pet groomers. Exposure via spray drift is not anticipated based on the current use patterns.

The most recent human health risk assessment for TCVP was completed in December 2015 (D. Drew *et al.*, 12/21/2015, *Tetrachlorvinphos (TCVP) Human Health Draft Risk Assessment (DRA) for Registration Review*, D411095). The current TCVP risk assessment reflects the following changes since the 2015 risk assessment:

- The reduction of the oral toxicological point of departure (POD) from 8.0 mg/kg/day to 2.8 mg/kg/day based on additional red blood cell (RBC) acetylcholinesterase (AChE) inhibition data identified during this re-evaluation in the current acute comparative cholinesterase assay (CCA) study in rats.

- The use of the literature study, Davis, M. et al., *Assessing Intermittent Pesticide Exposure from Flea Control Collars Containing the Organophosphorus Insecticide Tetrachlorvinphos.* Journal of Exposure Science and Environmental Epidemiology ((2008) 18, 564-57), (*hereinafter* Davis study), following approval for its use in risk assessment by the Human Studies Review Board (HSRB) in January 2016. Previously, risk estimates from both a surrogate residue transfer study (i.e., an amitraz pet collar study[1]) and the Davis literature study were presented. HED is now relying solely on the Davis study data since these chemical-specific data have been approved by the HSRB for use and result in a higher estimated exposure potential (i.e., are more health protective) than the surrogate data.

- Following a reassessment of the mutagenicity data available on TCVP, the relevance of the mutagenic findings to the tumorigenic response seen in female mice cannot be

[1] MRID 49468801: *Determination of Transferable Residues of Amitraz from the Hair of Dogs Following the Application of the Preventic® Collar.*

established. Therefore, a follow-up mouse micronucleus assay (OPPTS Harmonized Guideline 870.5395) is required for TCVP. Additionally, a study that investigates possible genotoxic activity in the target organ (liver) is required. This latter study should examine DNA damage potential (Comet assay, DNA adduct formation, or any other DNA target)[2].

- Following the Dec. 21, 2015 TCVP risk assessment, information was submitted during the public comment period to address whether the active ingredients in TCVP pet collars are released as a liquid or solid (dust) form, or both. The submitted information describes that both a liquid and particulate, or dust, are present on the surface of the pet collar. Therefore, HED has assumed that TCVP could be transferred in either form from the collar to the pet's fur and result in the potential for post-application exposures from contact with the treated pet. HED has assessed exposures resulting from the TCVP pet collar uses assuming that the TCVP pet collar product exists as a liquid and solid form concurrently at varying ratios (e.g., 1/99, 50/50, and 99/1 liquid/dust). [See Section 6.0 of this document for a complete description of this approach].

This document also addresses, where appropriate, the comments received during the public comment period following publication of the 2015 TCVP draft human health risk assessment. A comprehensive response to comments received is also provided in the following memo: D. Drew et al., *Tetrachlorvinphos (TCVP) Health Effects Division Response to Comments on the December 21, 2015 Draft Human Health Risk Assessment for TCVP Registration Review*, D433403, 12/21/2016).

Hazard

TCVP is a member of the OP class of pesticides. For TCVP, like other OPs, the initiating event in the adverse outcome pathway/mode of action (AOP/MOA) involves inhibition of the enzyme acetylcholinesterase (AChE) *via* phosphorylation of the serine residue at the active site of the enzyme. This inhibition leads to accumulation of acetylcholine and ultimately to neurotoxicity in the central and/or peripheral nervous system. For TCVP, AChE inhibition is the most sensitive endpoint in the toxicology database in multiple species, durations, lifestages, and routes. TCVP does not require metabolic activation to an oxon to inhibit AChE; i.e., the parent compound is the active form inhibiting AChE. OPs generally exhibit a phenomenon known as steady state AChE inhibition. After repeated dosing at the same dose, the degree of inhibition comes into equilibrium with the production of new, uninhibited enzyme. At this point, the amount of AChE inhibition at a given dose remains consistent across duration. In general, OPs reach steady state within 2-3 weeks; a pattern that is observed for most OPs, but not every OP, like TCVP, which shows no difference in response across duration. For TCVP the steady state is

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[2] N. McCarroll and D. Davis, 12/21/2016, Tetrachlorovinphos (TCVP): Revisit of Mutagenicity Studies, TXR#0057553, D437226.

reached after a single day of exposure. As such, the endpoint selection for TCVP considers data available for all durations of dosing when choosing the most protective point of departure.

The toxicology database for TCVP is complete except the requirement for additional mutagenicity studies [a follow-up mouse micronucleus assay (OPPTS Harmonized Guideline 870.5395) and an assay that examines possible genotoxic activity in the target (liver) organ] (McCarroll, 2016; TXR No. 0057226)[3]. TCVP has cholinesterase data across multiple lifestages, durations, and routes for both red blood cell (RBC) and brain cholinesterase inhibition. There are acceptable studies available for toxicity endpoint and point of departure (POD) selection. For TCVP, RBC AChE inhibition is the most sensitive endpoint and is the endpoint from which the PODs for all TCVP exposure routes and durations were selected.

There is no evidence of quantitative or qualitative sensitivity in the developmental rat and rabbit studies or in the gestational (fetus) or juvenile components of the comparative cholinesterase assay (CCA) studies in rats. AChE data from the CCA studies suggest that the fetus is not more sensitive than the pregnant dam, and that pregnant females are not more sensitive than non-pregnant females with respect to cholinesterase inhibition. When comparing RBC BMD_{10} (benchmark dose) estimates from across the acute (single dose) CCA and repeat dose CCA studies, it is apparent that there are no age-related (or duration-related) differences. The acute and steady state PODs selected for oral exposure risk assessment are based on RBC AChE inhibition in the postnatal day 11 (PND11) and postnatal day 21 (PND21) pups in the acute CCA since they provide the most robust dose-responses and are protective of all life stages. Although the steady state dietary POD was selected from an acute CCA, the acute study is considered appropriate for longer term durations since AChE data across the TCVP database demonstrate that there is no progression of AChE inhibition over exposure duration, and steady state inhibition occurs essentially after a single dose.

High quality AChE data for the dermal and inhalation routes are also available and allow for route specific evaluation. RBC AChE inhibition was observed in both sexes in the inhalation study (brain AChE was not assessed), while no inhibition of RBC or brain AChE was observed in the dermal study up to the limit dose. A non-cancer dermal assessment is not required for TCVP; however, a cancer dermal assessment is required. The dermal absorption factor is 9.6% for TCVP.

TCVP is classified as a Group C possible human carcinogen (based on statistically significant increases in combined hepatocellular adenoma/carcinoma in female mice) with a linear low-dose approach for quantification of risk using the oral slope factor (Q1*) of 1.83×10^{-3} $(mg/kg/day)^{-1}$. Whereas parent compound TCVP is the residue of concern for AChE inhibition, TCVP plus metabolites containing the 2,4,5 trichlorobenzene moiety are the residues of concern for cancer assessment. Following a reassessment of the mutagenicity data available on TCVP, it was determined that the relevance of the mutagenic findings to the tumorigenic response seen in

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[3] *Ibid.*

female mice cannot be established. Following the submission and review of the required mutagenicity assays, the need for an updated cancer assessment will be determined.

For TCVP, as for other OPs, the FQPA safety factor (SF) of 10X has been retained for infants, children, youths, and women of childbearing age for all exposure scenarios due to uncertainty in the human dose-response relationship for neurodevelopmental effects (see Section 4.5).

For the acute and steady state dietary assessments, a total uncertainty factor of 1000X is appropriate for infants, children, youths and females of childbearing age (10X to account for interspecies extrapolation and 10X for intraspecies variation and the 10X FQPA SF). The only population subgroup for dietary exposure scenarios for which the FQPA SF is not retained is adults 50-99 years of age; therefore, the total uncertainty factor for that population is 100X.

A total uncertainty factor of 1000X is appropriate for residential incidental oral exposures (10X for interspecies extrapolation, 10X for intraspecies variation, and a 10X FQPA SF). A total uncertainty factor of 300X is appropriate for all inhalation exposures: 3X for interspecies extrapolation, 10X for intraspecies variation, and a 10X FQPA SF for residential assessments (or a 10X database uncertainty factor for occupational assessments to protect potentially pregnant female workers) due to uncertainty in the human dose-response relationship for neurodevelopmental effects (see Section 4.5).

Tolerances

Tolerances for residues of TCVP are established under 40 CFR §180.252 for livestock commodities based on oral feed-through and direct dermal uses on livestock (cattle, swine, and poultry). The residues of concern for tolerance enforcement are tetrachlorvinphos, des-O-methyl tetrachlorvinphos, 1-(2,4,5-trichlorophenyl)ethanol (free and conjugated forms), 2,4,5-trichloroacetophenone, and 1-(2,4,5-trichlorophenyl)ethanediol (frequently abbreviated as TCVP, TCVPdeme, TCPEol , TCPEone, and TCPEdiol, respectively). The current tolerance expression under 40 CFR §180.252 includes all of these residues except des-O-methyl tetrachlorvinphos; this metabolite should be included in the tolerance expression. The current tolerance levels should be updated in the 40 CFR as discussed in Section 2.2.3.
There are no Codex maximum residue limits (MRLs) established or proposed for residues of TCVP. Canada has established MRLs for plant (apple and grape) and livestock commodities. The differences in U.S. and Canadian residue definitions prohibit harmonization.

Dietary Risk Assessment

Acute (TCVP), steady state (TCVP), and cancer (TCVP plus metabolites containing the 2,4,5 trichlorobenzene moiety) dietary (food and drinking water) exposure and risk assessments were conducted using the DEEM-FCID v3.16 model. The dietary exposure analyses for TCVP are mostly refined. The only food forms included in the analyses are based on animal commodities. The food residues were based upon U. S. Department of Agriculture's Pesticide Data Program (USDA PDP) monitoring data except where no appropriate PDP data were available (i.e.,

residues from poultry dermal application studies were used for poultry fat and skin). The Biological and Economic Analysis Division (BEAD) of OPP provided percent of livestock treated information. Model-derived estimated drinking water concentrations (EDWCs) were provided by the Environmental Fate and Effect Division (EFED). A distribution of EDWCs was used probabilistically in the acute and steady state analyses. For the cancer analysis, the EDWC was included as a single point estimate.

The acute dietary (food only) exposure analysis resulted in risk estimates above HED's level of concern (exceeded 100% the acute population adjusted dose (aPAD)) at the 99.9th percentile of exposure for the children's population subgroups. The highest exposed subgroup is children 3-5 years old at 190% of the aPAD. When drinking water is analyzed by itself, the acute dietary (water only) risk estimates are all below HED's level of concern for the U.S. population and all population subgroups at the 95th and 99.9th percentile of exposure.

The steady state (food only) exposure analysis resulted in risk estimates above HED's level of concern (exceeded 100% the steady state population adjusted dose (ssPAD)) at the 99.9th percentile of exposure for the children's population subgroups. The highest exposed subgroup is children 3-5 years old at 120% of the ssPAD. The steady state dietary (water only) risk estimates are all below HED's level of concern for the U.S. population and all population subgroups at the 95th and 99.9th percentile of exposure.

Residential Handler Risk Assessment

HED uses the term "handlers" to describe those individuals who are involved in the pesticide application process. HED believes that there are distinct tasks related to applications and that exposures can vary depending on the specifics of each task. Residential handlers are assumed to complete all elements of an application without use of any protective equipment.

Residential TCVP handler exposures are anticipated to be short- (1 to 30 days) and intermediate-term (1 to 6 months) in duration. However, because of the steady state AChE inhibition exhibited by the OPs (typically 21 days and longer for OPs, but 1 day to reach steady state for TCVP), steady state exposures were assessed and presented for residential exposures to TCVP pet products. Residential handler exposures to TCVP pet products may occur via the dermal or inhalation routes while the product is placed on a cat or dog. Both steady state non-cancer and cancer residential handler exposure assessments were performed for adult homeowners applying TCVP pet collars, dusts/powders, and pump/trigger sprays products to cats and dogs. Since there is no non-cancer dermal hazard for TCVP, the steady state (non-cancer) handler assessment includes only inhalation exposures. For the cancer assessment, both dermal and inhalation exposures are assessed.

<u>Residential Handler Steady State (Non-Cancer):</u>

Pet Collars: Because there is uncertainty as to whether the TCVP pet collars are liquid and/or dust formulated products, residential handler (adult) steady state inhalation exposures were evaluated assuming both liquid and dust residues are present simultaneously at varying ratios

(e.g., 1/99, 50/50, and 99/1 liquid/dust). Unit exposure (UE) data (for handler exposure), and residue transfer data and transfer coefficients (for post-application exposure) specific to each formulation type were used. For handlers, the liquid formulation assessment used spot-on surrogate UE data, which assumes negligible inhalation exposure; therefore, only the dust-specific UE data (i.e., a TCVP dust/powder applicator exposure study) is expected to result in the potential for inhalation exposures. In the case of handlers, therefore, the dust formulation drives any potential exposure. No non-cancer inhalation risks of concern were identified for residential handlers for any liquid/dust formulation ratio assumption (all MOEs ≥ level of concern (LOC) of 300). When assuming a ratio of 1/99 liquid/dust, MOEs range from 920 to 4,600; when assuming a ratio of 50/50 liquid/dust, MOEs range from 1,800 to 9,100; and when assuming a ratio of 99/1 liquid/dust, MOEs range from 91,000 to 450,000.

Dust/Powder and Pump/Trigger Spray: All residential handler (adult) non-cancer steady state inhalation risks estimated for the TCVP pet dust/powder and pump/trigger spray formulations are not of concern (i.e., all MOEs are > 300; LOC = 300; range = 3,200 to 160,000).

Residential Handler Cancer:

Pet Collars: Residential handler cancer risks (combined dermal and inhalation) estimated for TCVP pet collars assuming 1/99 and 50/50 liquid/dust formulation ratios are all 10^{-7}. When assuming a 99/1 liquid/dust formulation for pet collars, the residential handler cancer risk estimates are all 10^{-8}.

Dust/Powder and Pump/Trigger Spray: Residential handler estimated cancer risks (combined dermal and inhalation) for TCVP dusts/powders range from 10^{-9} to 10^{-7}, and for pump/trigger sprays range from 10^{-9} to 10^{-8}.

Residential Post-Application Risk Assessment

There is the potential for post-application exposure for individuals exposed as a result of contacting a cat or dog previously treated with TCVP pet products (dusts/powders, pump/trigger sprays, pet collars). Since there is no non-cancer dermal hazard for TCVP, a quantitative non-cancer post-application dermal exposure assessment was not performed for adults or children. A quantitative residential post-application inhalation exposure assessment was not performed as inhalation exposure is expected to be negligible from applications to pets. The quantitative exposure/risk assessment for residential post-application exposures is based on incidental oral (hand-to-mouth) exposure to children (1 to < 2 years old) from contacting cats and dogs treated with TCVP. While not the only lifestage potentially exposed for these post-application scenarios, this lifestage is health protective for the exposures and risk estimates for any other potentially exposed lifestage.

Residential TCVP post-application exposures are anticipated to be short- (1 to 30 days), intermediate-term (1 to 6 months), and long-term (>6 months – *for pet collar scenarios only*) in duration. However, because of the steady state AChE inhibition exhibited by the OPs, steady state exposures were assessed and presented for residential exposures to TCVP pet products.

Residential Post-Application Steady State (Non-Cancer):

Pet Collars: As was done for residential handlers, due to the uncertainty as to whether the TCVP pet collars are liquid and/or dust formulated products, residential post-application exposures were evaluated assuming both liquid and dust residues are present simultaneously at varying ratios (e.g., 1/99, 50/50, and 99/1 liquid/dust). For post-application exposure from pet collars, the same data were used to estimate transferable residues for both liquid and dust formulations; however, the transfer coefficients used to assess potential post-application exposure to dust formulations are much higher compared to those used for liquid formulations. Therefore, as with handlers, the post-application risk estimates are driven by the presence of dust in the formulations. Children's incidental oral (hand-to-mouth) steady state exposures to pets treated with TCVP collars are estimated to be of concern regardless of the ratio of liquid/dust assumed (i.e., MOEs < 1000; LOC = 1000). When assuming a 1/99 liquid/dust formulation ratio, MOEs range from 0.91 to 7.4. When assuming a 50/50 liquid/dust formulation, MOEs range from 1.8 to 15, and when assuming a 99/1 liquid/dust formulation, MOEs range from 65 to 530.

Dust/Powder and Pump/Trigger Spray: Children's incidental oral (hand-to-mouth) steady state exposures to pets treated with TCVP dust/powders are estimated to be of concern (MOEs range from 98 to 640; LOC = 1000). However, children incidental oral exposures to pets treated with TCVP pump/trigger spray products are estimated not to be of concern (i.e., MOEs are > 1000; MOEs range from 1,600 to 15,000).

Residential Post-Application (Cancer):

Pet Collars: Residential post-application cancer (adult; dermal only as post-application inhalation exposure is negligible for this use) risk estimates for TCVP pet collars assuming 1/99 or 50/50 liquid/dust formulation ratios range from 10^{-5} to 10^{-4}. When assuming a 99/1 liquid/dust formulation ratio, cancer risk estimates range from 10^{-6} to 10^{-5}.

Dust/Powder and Pump/Trigger Spray: Residential post-application cancer (adult; combined dermal and inhalation) risks estimated for TCVP dust/powder products range from 10^{-7} to 10^{-6}, and for TCVP pump/trigger sprays are all 10^{-7}.

Spray Drift

A quantitative spray drift assessment was not conducted because the use of TCVP for direct animal treatment to livestock and their premises, in kennels, outdoors as a perimeter treatment, and as a flea treatment on cats and dogs are either 1) not applied via aircraft, groundboom, or airblast equipment or 2) for applications to poultry buildings with groundboom equipment, the use is indoors and not anticipated to be a significant source of spray drift.

Aggregate Risk Assessment

The acute aggregate risk assessment combines exposures to TCVP from food and drinking water. There are acute risk estimates of concern for food only; therefore, a quantitative acute aggregate

risk assessment was not conducted. The steady state aggregate assessment includes the steady state dietary (food and drinking water) and residential exposures. However, because there are risks of concern associated with both dietary (food) and residential exposure, a quantitative steady state aggregate risk assessment was not conducted. If mitigation occurs such that the risks for the individual contributors to the aggregate risk are acceptable, a quantitative assessment may be completed at that time.

The cancer aggregate risk assessment combines residential and dietary (food and drinking water) expected lifetime exposures for adults. For TCVP, a cancer aggregate assessment was performed for adult handlers and for adult post-application activities related to residential pet product use.

The residential handler cancer aggregate assessment uses exposures from applying TCVP products to pets. The cancer aggregate assessment combines the highest (worst case, upper bound) handler exposure for each pet product formulation type with dietary exposure; this results in aggregate cancer risk estimates that are protective of exposures to other registered pet products of the same formulation type. The cancer aggregate (dietary and residential exposures) risk estimates for handlers for the upper bound exposures for collars, dust/powders, and pump/trigger sprays are in the 10^{-7} to 10^{-6} range

The residential post-application cancer aggregate assessment uses exposures from contacting pets treated with TCVP products. The cancer aggregate assessment combines the highest (worst case, upper bound) post-application exposure for each pet product formulation type with dietary exposure; this results in aggregate cancer risk estimates that are protective of exposures to other registered pet products of the same formulation type. The cancer aggregate (dietary and residential exposures) post-application risk estimates for the upper bound exposures for collars, dust/powders, and pump/trigger sprays range from 10^{-6} to 10^{-4}.

Occupational Handler Risk Assessment

HED uses the term handlers to describe those individuals who are involved in the pesticide application process. HED believes that there are distinct job functions or tasks related to applications and exposures can vary depending on the specifics of each task. Job requirements (amount of chemical used in each application), the kinds of equipment used, the target being treated, and the level of protection used by a handler can cause exposure levels to differ in a manner specific to each application event. Occupational handler exposures to TCVP may occur via the dermal or inhalation routes while the mixing/loading and applying products registered for dermal or oral treatment to livestock and their premises, in kennels, outdoors as a perimeter treatment, and as a flea treatment on cats and dogs (professional pet handlers).

Occupational handler exposure is expected to be short- and intermediate-term in duration. However, because of the steady state AChE inhibition exhibited by the OPs, steady state exposures were assessed and presented for occupational exposures to TCVP products. Both steady state non-cancer and cancer handler exposure assessments were performed. Since there is no non-cancer dermal hazard for TCVP, the steady state (non-cancer) handler assessment

includes only inhalation exposures. For the cancer assessment, both dermal and inhalation exposures are assessed.

Occupational Handler Steady State (Non-Cancer):

Of the 198 total occupational handler exposure scenarios assessed, the majority (162) are not of concern (i.e., steady state inhalation MOEs are $\geq$ 300; LOC = 300) with currently required personal protective equipment (PPE) (i.e., respiratory protection). Of the remaining 36 handler exposure scenarios, an additional 25 are not of concern with consideration of increasing levels of respiratory protection (i.e., 11 occupational handler exposure scenarios result in estimated risks of concern despite the addition of respiratory protection or engineering controls).

Occupational Handler Cancer:

Occupational cancer risks were estimated for both private/farmer and contract/commercial handlers. Cancer risk estimates, with currently required PPE, range from 10^{-10} to 10^{-5} for private/farmer handlers and from 10^{-10} to 10^{-4} for contract/commercial handlers.

Occupational Post-Application Risk Assessment

HED uses the term post-application to describe exposures that occur when individuals are present in an environment that has been previously treated with a pesticide (also referred to as re-entry exposure). Such exposures may occur when workers enter previously treated areas to perform job functions, including activities related to crop production, such as scouting for pests or harvesting. Post-application exposure levels vary over time and depend on such things as the type of activity, the nature of the crop or target that was treated, the type of pesticide application, and the chemical's degradation properties.

Occupational post-application exposures are not anticipated for TCVP as the majority of application scenarios are not to foliar surfaces. The use of TCVP outdoors as a perimeter treatment is not expected to result in occupational post-application exposure as reentry activities related to crop production (e.g., scouting, harvesting) are not anticipated for this use pattern.

Human Studies Review

This risk assessment relies in part on data from studies in which human subjects were intentionally exposed to a pesticide or other chemical. These data, which include studies from Pesticide Handler Exposure Database (PHED) 1.1; the AHETF database; the Residential SOPs (Treated Pets); as well as a TCVP dust/powder applicator exposure study (MRID 45519601), a mixer/loader/applicator wettable powder study (MRID 42622301), and TCVP dust and pump spray study (MRID 45485501): (1) are subject to ethics review pursuant to 40 CFR Part 26, (2) have received the review necessary for consideration in this risk assessment, and (3) are compliant with applicable ethics requirements. For certain studies, the ethics review may have

included review by the HSRB. Descriptions of data sources, as well as guidance on their use, can be found at the agency website.[4]

Data were also used from a literature study using TCVP pet collars, Davis, M. *et. al., Assessing Intermittent Pesticide Exposure from Flea Control Collars Containing the Organophosphorus Insecticide Tetrachlorvinphos.* Journal of Exposure Science and Environmental Epidemiology. (2008) 18, 564-57). On January 12-13, 2016 the EPA HSRB met to address the scientific and ethical charge questions related to the Davis study. The HSRB concluded that, "the research is scientifically sound and, if used appropriately, the pet fur transferable residue data from the rubbing protocol used in the study can provide useful information for evaluating potential exposures of adults and children from contact with dogs treated with tetrachlorvinphos containing pet collars."[5]

CropLife America Petition

On November 29, 2016, CropLife America (CLA) submitted a petition to EPA asking the agency to "halt regulatory decisions that are highly influenced/determined by results of epidemiological studies that do not meet well-defined data quality standards, and that are not integrated into the health risk assessment in a transparent, well-defined manner." Any interim or final registration review decision for TCVP could potentially be impacted by EPA consideration of the epidemiological studies identified in the CLA petition. EPA is therefore placing a copy of the CLA petition in the registration review docket for TCVP. In the near future, EPA intends to publish a notice on its Pesticide Website announcing the receipt of the CLA petition and opening a comment period on the petition. Persons wishing to comment on the petition should respond to EPA in connection with that comment period.

2.0 HED Recommendations

2.1 Data Deficiencies

A follow-up mouse micronucleus assay (OPPTS Harmonized Guideline 870.5395) and a study that investigates possible genotoxic activity in the target organ (liver) are required. This latter study should examine DNA damage potential (Comet assay, DNA adduct formation, or any other DNA target).

Based on the findings from the mutagenicity revisit, HED is recommending that TCVP be assayed in a follow-up mouse micronucleus assay (OPPTS Harmonized Guideline 870.5395)

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[4] https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/occupational-pesticide-handler-exposure-data and https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/occupational-pesticide-post-application-exposure

[5] Letter from Liza Dawson, PhD, Chair of the EPA HSRB to Thomas Burke, PhD, MPH, EPA Science Advisor. Subject: January 12-13, 2016 EPA Human Studies Review Board Meeting Report. March 30, 2016.

using both sexes, an appropriate sample size (5/sex/dose/sacrifice time) and oral treatment (dietary would be the best fit for the risk assessment). HED further recommends that the assay should cover the range of doses used in the 1980 Hazleton study (MRID 00117443) that will span the tumorigenic dose range for both sexes and the conditions should simulate conditions in the Amer et al., 1983 study. An additional study which would investigate possible genotoxic activity in the target organ (*i.e.*, mouse liver) should be performed. This assay with the target tissue would be appropriate and should follow a similar protocol as described above and should examine DNA damage potential (*e.g.*, Comet assay, DNA adduct formation or any other DNA target)[6].

2.2 Tolerance Considerations

2.2.1 Enforcement Analytical Method

A gas liquid chromatography (GLC) method for the determination of TCVP *per se* in livestock commodities is described in the Pesticide Analytical Method (PAM), Vol. II, as Method I.

The registrant has submitted a method (14020.6106) for the determination of tetrachlorvinphos and its metabolites (TCVPdeme, TCPEdiol, TCPEone and TCPEol) in livestock commodities, which uses QuEChERS and LC/MS/MS methods. The test data for method 14020.6106 are classified as scientifically acceptable for use as an analytical method for ruminant and poultry commodities.

The submitted multiresidue method testing data are acceptable and indicate that FDA multiresidue methods are not suitable for analysis of the TCVP metabolites TCPEdiol and TCVPdeme. However, the metabolites TCPEol and TCPEone were recoverable under Protocol F, although fortified recoveries were small (<50%).

It should be noted that the FDA PESTDATA database dated 8/93 (PAM Vol. I, Appendix II) indicates that parent compound TCVP is completely recovered (>80%) using FDA multiresidue method protocol D (section 232.4) but is not recovered using protocol E (Sections 211.1/231.1 and 212.1/232.1, fatty and nonfatty matrices).

2.2.2 International Harmonization

There are no Codex maximum residue limits (MRLs) established or proposed for residues of TCVP. Canada has established MRLs for plant (apple and grape) and livestock commodities. The U.S. tolerances are for livestock commodities; there are no registered crop uses. Canada's residue definition is 2-chloro-1-(2,4,5-trichlorophenyl) vinyl dimethyl phosphate (TCVP) and its

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[6] N. McCarroll and D. Davis, 12/21/2016, Tetrachlorovinphos (TCVP): Revisit of Mutagenicity Studies, TXR#0057553, D437226.

low melting isomer as opposed to the U.S. definition which includes the parent compound TCVP plus the four metabolites of concern. The differences in U.S. and Canadian residue definitions prohibit harmonization. HED has not examined the Canadian registrations; different use patterns may also be a factor in achieving harmonization. A summary of U.S. and international tolerances and maximum residue limits is presented in Appendix F.

2.2.3 Recommended Tolerances

Tolerances for residues of TCVP in livestock commodities are established under 40 CFR §180.252. The current tolerance expression is for the combined residues of tetrachlorvinphos [(Z)-2-chloro-1-(2,4,5-trichlorophenyl)vinyl dimethyl phosphate] and its metabolites, 1-(2,4,5-trichlorophenyl)-ethanol (free and conjugated forms), 2,4,5-trichloroacetophenone, and 1-(2,4,5-trichlorophenyl)-ethanediol.

The HED Metabolism Committee has determined that the residues of concern for tolerance enforcement are tetrachlorvinphos, des-O-methyl tetrachlorvinphos, 1-(2,4,5-trichlorophenyl)ethanol (free and conjugated forms), 2,4,5-trichloroacetophenone, and 1-(2,4,5-trichlorophenyl)ethanediol. The current tolerance expression under 40 CFR §180.252 includes all of these residues *except des-O-methyl tetrachlorvinphos*; this metabolite should be included in the tolerance expression. To allow separate risk assessments for 1) cholinesterase inhibition (parent TCVP only) and 2) carcinogenicity (parent plus metabolites), the tolerances for each livestock commodity should also specify the maximum residues of TCVP *per se* from the total residues. The tolerance definition should be modified as follows, to be consistent with the Tolerance Expression Guidance issued 5/27/09 (S. Knizner).

Tolerances are established for residues of the insecticide tetrachlorvinphos, including its metabolites and degradates, in or on the commodities in the table below. Compliance with the tolerance levels specified below is to be determined by measuring only the sum of tetrachlorvinphos [(Z)-2-chloro-1-(2,4,5-trichlorophenyl)vinyl dimethyl phosphate) and its metabolites chloro- 1 -(2,4,5-trichlorophenyl)-vinylmonomethyl phosphate, 1-(2,4,5-trichlorophenyl)-ethanol (free and conjugated forms), 2,4,5-trichloroacetophenone, and 1-(2,4,5-trichlorophenyl)-ethanediol, calculated as the stoichiometric equivalent of tetrachlorvinphos, in or on the commodity.

Table 2.2.3. Tolerance Reassessment Summary for Tetrachlorvinphos.

Commodity	Established Tolerance [1] (ppm)	Maximum Residues [2] (ppm)	Reassessed Tolerance [3,4] (ppm)	Comments; *Correct Commodity Definition*
Cattle, fat (of which no more than 0.1 ppm is tetrachlorvinphos *per se*)	0.2	0.84 (0.56) subcutaneous fat; 0.75 (0.34) peritoneal fat	1.0	*Cattle, fat (of which no more than 0.6 ppm is tetrachlorvinphos per se)*

Table 2.2.3. Tolerance Reassessment Summary for Tetrachlorvinphos.				
Commodity	Established Tolerance [1] (ppm)	Maximum Residues [2] (ppm)	Reassessed Tolerance [3,4] (ppm)	Comments; *Correct Commodity Definition*
Cattle, kidney (of which no more than 0.05 ppm is tetrachlorvinphos *per se*)	1.0	--	Remove	See cattle, meat byproducts
Cattle, liver (of which no more than 0.05 ppm is tetrachlorvinphos *per se*)	0.5	--	Remove	
Cattle, meat (of which no more than 2.0 ppm is tetrachlorvinphos *per se*)	2.0	0.27 (0.21) muscle	0.3	*Cattle, meat (of which no more than 0.2 ppm is tetrachlorvinphos per se)*
Cattle, meat by products, except kidney and liver	1.0	--	Remove	See cattle, meat byproducts
Cattle, meat by products	None	0.16 (<0.01) liver; 0.28 (0.015) kidney; 0.84 (0.56) subcutaneous fat; 0.75 (0.34) peritoneal fat; 0.27 (0.21) muscle	1.0	*Cattle, meat byproducts (of which no more than 0.6 ppm is tetrachlorvinphos per se)* [5]
Egg (of which no more than 0.05 ppm is tetrachlorvinphos *per se*)	0.2	0.288 (0.026)	0.3	*Egg (of which no more than 0.03 ppm is tetrachlorvinphos per se)*
Hog, fat (of which no more than 0.1 ppm is tetrachlorvinphos *per se*)	0.2	0.84 (0.56) subcutaneous fat; 0.75 (0.34) peritoneal fat	1.0	*Hog, fat (of which no more than 0.6 ppm is tetrachlorvinphos per se)*
Hog, kidney (of which no more than 0.05 ppm is tetrachlorvinphos *per se*)	1.0	--	Remove	See hog, meat byproducts
Hog, liver (of which no more than 0.05 ppm is tetrachlorvinphos *per se*)	0.5	--	Remove	
Hog, meat (of which no more than 2.0 ppm is tetrachlorvinphos *per se*)	2.0	0.27 (0.21) muscle	0.3	*Hog, meat (of which no more than 0.2 ppm is tetrachlorvinphos per se)*
Hog, meat byproducts, except kidney and liver	1.0	--	Remove	See hog, meat byproducts
Hog, meat by products	None	0.16 (<0.01) liver; 0.28 (0.015) kidney; 0.84 (0.56) subcutaneous fat; 0.75 (0.34) peritoneal fat; 0.27 (0.21) muscle	1.0	*Hog, meat byproducts (of which no more than 0.6 ppm is tetrachlorvinphos per se)* [5]

Table 2.2.3. Tolerance Reassessment Summary for Tetrachlorvinphos.				
Commodity	Established Tolerance [1] (ppm)	Maximum Residues [2] (ppm)	Reassessed Tolerance [3,4] (ppm)	Comments; *Correct Commodity Definition*
Milk, fat (reflecting negligible residues in whole milk and of which no more than 0.05 ppm is tetrachlorvinphos *per se*)	0.05	0.072 (0.036) for milk; 0.078 (<0.01) for cream	0.1	*Milk (of which no more than 0.04 ppm is tetrachlorvinphos per se)*
Poultry, fat (of which no more than 7.0 ppm is tetrachlorvinphos *per se*)	7.0	1.298 (0.099) abdominal fat	1.4	*Poultry, fat (of which no more than 0.1 ppm is tetrachlorvinphos per se)*
Poultry, liver (of which no more than 0.05 ppm is tetrachlorvinphos *per se*)	2.0		Remove	See poultry, meat byproducts
Poultry, meat (of which no more than 3.0 ppm is tetrachlorvinphos *per se*)	3.0	0.40 (0.082) muscle	0.4	*Poultry, meat (of which no more than 0.1 ppm is tetrachlorvinphos per se)*
Poultry, meat byproducts, except liver	2.0	--	Remove	See poultry, meat byproducts
Poultry, meat byproducts	None	0.52 (0.016) liver; 0.58 (0.022) kidney; 0.40 (0.082) muscle; 19.41 (6.03) skin with fat; 1.30 (0.099) abdominal fat	20	*Poultry, meat byproducts (of which no more than 6.0 ppm is tetrachlorvinphos per se)* [5]

[1] Time-limited tolerances; current tolerance expression is for the combined residues of tetrachlorvinphos [(Z)-2-chloro-1-(2,4,5-trichlorophenyl)vinyl dimethyl phosphate] and its metabolites, 1-(2,4,5-trichlorophenyl)-ethanol (free and conjugated forms), 2,4,5-trichloroacetophenone, and 1-(2,4,5-trichlorophenyl)-ethanediol; expression should also include des-O-methyl tetrachlorvinphos.

[2] Total residues of tetrachlorvinphos and its metabolites, TCVP-deme, TCPEone, TCPEol (free and conjugated forms), and TCPEdiol (free and conjugated), expressed in terms of parent equivalents; the value in parentheses represents the maximum residues of the parent tetrachlorvinphos.

[3] Reassessed tolerance is based on the maximum residue from the respective magnitude of the residue study; the maximum residues of the parent tetrachlorvinphos are reported in the corrected commodity definition.

[4] The residue data for cattle can be used to set tolerances for hog commodities since residues in hog tissues are not likely to be greater than those in cattle tissues.

[5] According to the 18 July 2007 Minutes of the HED ChemSAC meeting, the guidance document will be revised to include language detailing the use of the highest residue data for any tissue (liver, kidney, fat, skin or muscle) to determine the tolerance for meat byproducts. A single tolerance on "meat byproducts" will be recommended based on that highest residue, and individual tolerances will no longer be set on liver, kidney, or meat byproducts (except liver and kidney).

2.3 Label Recommendations

2.3.1 Recommendations from Residue Reviews

The following label revisions are recommended based on the application methods and rates used in the tetrachlorvinphos magnitude of the residue studies, which were used to determine the appropriate tolerance levels in livestock commodities (GLN 860.1200 Directions for Use):

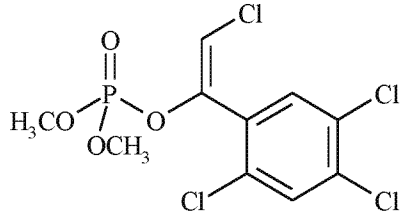
- Based on the magnitude of the residue study on cattle, the product labels with direct animal spray uses on cattle (EPA Reg. Nos. 61483-43 and 61483-50) should be amended to specify a maximum of three applications, with two-week retreatment intervals, at 19 g ai/animal/dose. The product label for Ravap (EPA Reg. No. 61483-50) should also be amended to provide conversion factors to allow calculation of direct animal spray treatment rate in terms of g ai/animal.

- Based on the magnitude of the residue study on poultry, the product labels with direct animal spray uses on poultry (EPA Reg. Nos. 61483-43 and 61483-50) should be amended to specify a maximum of seven applications (with two-week retreatment intervals) at 0.18 g ai/hen/application. Note that the label should specify the weight or volume of the product to be applied.

3.0 Introduction

3.1 Chemical Identity

Table 3.1. Tetrachlorvinphos Nomenclature.

Compound	
Common name	Tetrachlorvinphos
Company experimental name	TCVP
IUPAC name	(Z)-2-chloro-1-(2,4,5-trichlorophenyl) vinyl dimethyl phosphate
CAS registry number	22248-79-9

See Appendices D and E for nomenclature and physical/chemical properties of TCVP and metabolites (TCVPdeme, TCPEdiol, TCPEone and TCPEol, TCCEol, TCBA).

3.2 Physical/Chemical Characteristics

Technical tetrachlorvinphos is a tan to brown crystalline solid with a melting point of 93-98 °C. TCVP is not expected to volatilize significantly due to a low vapor pressure of 2.6×10^{-7} torr (25°C). The solubility of tetrachlorvinphos in water at 25°C is 11.6 mg/L. TCVP has limited solubility in most aromatic hydrocarbons. TCVP is hydrophobic, with an octanol-water partition coefficient of 3350 (Log K_{ow} of 3.53).

3.3 Pesticide Use Pattern

TCVP is used as a direct animal treatment to livestock (i.e., cattle, horses, poultry and swine) and their premises, in kennels, outdoors as a perimeter treatment, and as a flea treatment on cats and dogs. The TCVP livestock and perimeter treatment uses are formulated as follows: dusts (D), emulsifiable concentrates (EC), feed through (solid, granular and pelleted/tableted) and liquid food additives), feed blocks, and wettable powders (WP). TCVP can be applied by a variety of means/equipment types including: backrubber/facerubber; backpack; cup; groundboom; handheld fogger; manually-pressurized handwand; mechanically-pressurized handwand; open pour (dust and liquid formulations); paint (airless sprayer or brush/roller); pet collar; plunger; rotary duster; shaker can; spoon; stationary fogger; and trigger spray. For a complete list of registered uses, including maximum use rates, see Appendix A of D436833 (W. Britton, 12/2016, *Tetrachlorvinphos: Final Occupational and Residential Exposure Assessment for Registration Review*).

3.4 Anticipated Exposure Pathways

Humans may be exposed to TCVP residues in food since TCVP may be directly applied to, or fed to, livestock which may result in residues in animal commodities. TCVP may reach surface and ground water sources of drinking water through the outdoor usage on poultry droppings, garbage and manure piles, and kennels and corrals. Residential exposures (handler and post-application) may occur as a result of the application to dogs and cats as dust/powders, sprays, or collars. In an occupational setting, applicators may be exposed while handling the pesticide prior to application, as well as during application. Occupational post-application exposures are not expected as reentry activities are not anticipated for the registered TCVP uses.

3.5 Consideration of Environmental Justice

Potential areas of environmental justice concerns, to the extent possible, were considered in this human health risk assessment, in accordance with U.S. Executive Order 12898, "Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations," http://www.epa.gov/compliance/environmentaljustice/resources/policy/exec_order_12898.pdf. As a part of every pesticide risk assessment, OPP considers a large variety of consumer subgroups according to well-established procedures. In line with OPP policy, HED estimates risks to population subgroups from pesticide exposures that are based on patterns of that subgroup's food and water consumption, and activities in and around the home that involve pesticide use in a residential setting. Extensive data on food consumption patterns are compiled by the USDA under the National Health and Nutrition Survey/What We Eat in America (NHANES/WWEIA) and are used in pesticide risk assessments for all registered food uses of a pesticide. These data are analyzed and categorized by subgroups based on age and ethnic group. Additionally, OPP is able to assess dietary exposure to smaller, specialized subgroups and exposure assessments are performed when conditions or circumstances warrant. Whenever appropriate, non-dietary exposures based on home use of pesticide products and associated risks

for adult applicators and for toddlers, youths, and adults entering or playing on treated areas post-application are evaluated. Further considerations are currently in development as OPP has committed resources and expertise to the development of specialized software and models that consider exposure to bystanders and farm workers as well as lifestyle and traditional dietary patterns among specific subgroups.

4.0 Hazard Characterization and Dose-Response Assessment

TCVP is a member of the organophosphate class of pesticides. Like other OPs, the initiating event in the adverse outcome pathway/mode of action (AOP/MOA) for TCVP involves inhibition of the enzyme AChE *via* phosphorylation of the serine residue at the active site of the enzyme. This inhibition leads to accumulation of acetylcholine and ultimately to neurotoxicity in the central and/or peripheral nervous system (see Figure 1). TCVP is in the oxon form and does not require bioactivation prior to inhibiting AChE. For TCVP, AChE inhibition is the most sensitive endpoint in the toxicology database in multiple species, durations, lifestages, and routes. AChE inhibition is the focus of this hazard characterization; the availability of reliable AChE inhibition dose response data is one of the key determinants in evaluating this toxicology database.

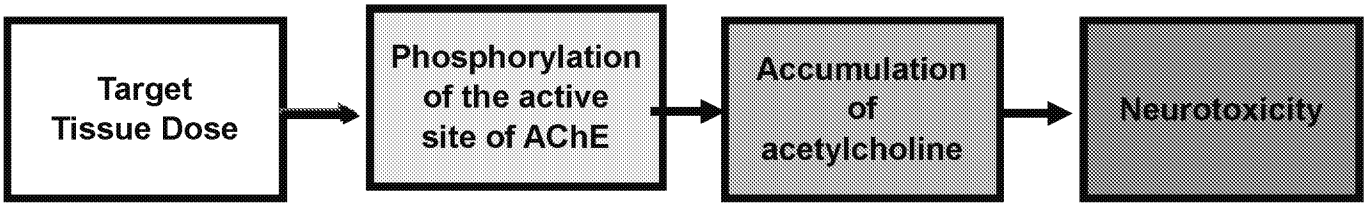


Figure 1. Adverse outcome pathway for OPs

4.1 Toxicology Studies Available for Analysis

The toxicology database for TCVP is complete except for a follow-up mouse micronucleus assay (OPPTS Harmonized Guideline 870.5395) and an *in vivo* assay to examine DNA damage potential (*e.g.*, Comet assay, DNA adduct formation, or any other DNA target)[7].

There are acceptable studies available for toxicity endpoint selection; they include:

- subchronic oral toxicity studies in rats
- chronic oral toxicity studies in rats and dogs
- carcinogenicity studies in rats and mice
- developmental studies in rats and rabbits
- reproduction study in rats

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[7] *Ibid.*

- acute and subchronic neurotoxicity studies in rats
- developmental neurotoxicity (DNT) study in rats
- acute and repeated comparative (CCA) cholinesterase (ChE) studies in juvenile and adult rats
- repeated, gestational ChE study in pregnant rats and fetuses
- delayed neurotoxicity study in hens
- subchronic dermal toxicity study in rats
- repeated dosing inhalation toxicity study in rats
- immunotoxicity study in mice
- complete mutagenicity study battery
- dermal penetration study in rats
- metabolism study in rats

4.2 Absorption, Distribution, Metabolism, & Excretion (ADME)

TCVP, unlike some other OPs, does not require metabolic activation to the oxon form to inhibit AChE. In a rat metabolism study, TCVP was almost completely metabolized, and most of the radiolabel was excreted in the urine (46%-60%) and feces (38%-56%) within 48 hours of dosing. Only minor amounts (>0.5%) were found in the tissues. Very little un-metabolized parent compound was recovered. The major metabolite in feces was trichlorophenylethanol, with lesser amounts of trichlorophenylethandiol. The major metabolite in urine was trichloromandelic acid, with lesser amounts of desmethyl tetrachlorvinphos. There is no evidence of bioaccumulation. Some differences in metabolism were noted between the sexes; *e.g.,* males excreted more trichloromandelic acid, a more completely metabolized form of TCVP, whereas females excreted more of the desmethyl TCVP, which could be derived from TCVP with only a single metabolic step.

4.2.1 Dermal Absorption

There is a dermal absorption study in rats, which provides a dermal absorption factor (DAF) of 9.6%. In an acceptable *in vivo* dermal penetration study in rats (MRID 42111501), male rats were treated at 0.01, 0.1, 1, and 5 mg/cm^2 and sacrificed at 0.5, 1, 2, 4, or 10 hours post dose. Based on total amount of radioactivity recovered from urine, tissues, feces, and carcass after 10 hours of dermal exposure, 84% of the applied dose (0.1 mg/cm^2) was recovered in the wash and 9.57% was in the skin, urine, feces, and carcass. The DAF was used to evaluate dermal exposures in the cancer risk assessment. However, since there was no dermal hazard identified for non-cancer endpoints in the dermal toxicity study on TCVP; *i.e.,* no AChE inhibition at the limit dose and no concern for increased susceptibility after repeat exposure, a quantitative dermal assessment was not performed (see Section 4.6.1).

4.3 Toxicological Effects

AChE inhibition is the well-established cholinergic mode of action for OPs and is typically used as the critical effect in hazard characterization for members of this class of pesticides. TCVP inhibits AChE in various species including rats, mice, rabbits, and dogs and is the most sensitive effect in the database. TCVP has AChE data across multiple lifestages (fetal, post-natal, adult), durations (single to 104 weeks), and routes (oral, dermal, inhalation) for both red blood cell (RBC) and brain AChE inhibition. However, when looking at the AChE inhibition data across the numerous studies and datasets, it is apparent that there is no consistent pattern as to the relative sensitivity of the RBC and brain compartments, sex, or life stage. For instance, at a single dose of 10 mg/kg, male RBC and brain AChE were similarly inhibited in both adults (-17% and -13% respectively) and PND11 pups (-14% and -14%, respectively). Additionally, as is observed for some OPs, the oral AChE data demonstrate no increase in inhibition with repeated exposures as compared to a single dose. Specifically, the acute single dose CCA data show BMD_{10} of 6.5, with the 11-day repeated exposure BMD_{10} of 7.7 in adult male rats (see Section 4.3.2).

Transient clinical signs [gait alterations, constricted pupils, tremors (fore- and hindlimb), body cool to the touch, decreased defecation, red material on forelimbs, around eyes, nose, mouth] characteristic of cholinergic toxicity were observed in the acute neurotoxicity rat study, and tremors were observed in pregnant rats in the developmental toxicity study at dose levels 100X higher and 5X higher than those eliciting AChE inhibition, respectively. The hen study was negative for indications of delayed neurotoxicity.

There is no evidence of quantitative or qualitative sensitivity in the developmental rat and rabbit studies or in the rat reproduction study following pre-natal and/or postnatal exposure to TCVP. In the rat developmental toxicity study, no developmental effects were observed in the fetus. Developmental toxicity (increased early resorptions, post-implantation loss, and decreased number of live fetuses) was observed in the rabbit developmental toxicity study at the same dose level where significant toxicity (mortality, abortion) was observed in the maternal rabbit. No reproductive or offspring toxicity was observed in the 2-generation reproductive rat study, but increased adrenal weights were observed in the parental rats.

AChE data from the CCA study suggest that the fetus is not more sensitive than the pregnant dam, and that pregnant females are not more sensitive than non-pregnant females with respect to cholinesterase inhibition. When comparing RBC BMD_{10} estimates from across the repeat (48773401) and acute studies (48773401a), it is apparent that there are no age-related (or duration-related) differences. For instance, the BMD_{10} estimates range from 3.2 mg/kg in PND21 male rats to 5.0 mg/kg in PND11 male rats and to 6.5 mg/kg in adult males in the acute CCA study and from 8.6 mg/kg/day in adult female to 20.5 mg/kg/day in the PND 11 pups in the repeat CCA study. Furthermore, the points of departure (POD) used for risk assessment, which are based on cholinesterase inhibition in the PND11 and PND21 animals, since they provide the most robust BMD and BMDL dose-responses, are protective of all life stages.

In the developmental neurotoxicity study (DNT), quantitative susceptibility was observed in pups (decreased pup weight, decreased relative brain weight/measurements) but only at the high

dose of 200 mg/kg/day where maternal toxicity was not demonstrated. However, a 200 mg/kg/day dose to adult female rats in the repeat dose CCA study resulted in 62% RBC and 57% brain cholinesterase inhibition, indicating significant toxicity occurred in the dam in the DNT at this dose. The 200 mg/kg/day dose to the juvenile rats is 20-fold higher than doses reflecting approximately 10%-20% inhibition in juvenile pups in the CCA study and 70-fold higher than the point of departure. Therefore, when considered in combination with the results from the CCA, the high dose of the DNT is not of concern for risk assessment. The BMDs relied upon from the CCA study are protective of the effects observed in pups at higher doses in the DNT study.

TCVP is classified as a Group C possible human carcinogen with a linear low-dose approach for quantification of risk using the oral slope factor (Q1*) of 1.83×10^{-3}.

In acute lethality studies, TCVP has low acute toxicity by the oral, dermal, and inhalation routes of exposure. It is a slight dermal irritant, a moderate eye irritant, and a dermal sensitizer.

4.3.2 Critical Durations of Exposure

One of the key elements in risk assessment is the appropriate integration of temporality between the exposure and hazard assessments. One advantage of an AOP understanding is that human health risk assessments can be refined and focused on the most relevant durations of exposure. The following text provides an analysis of the temporal pattern of AChE inhibition from acute, single dosing, and repeated dosing studies in laboratory animals for TCVP. This analysis provides the basis for determining which exposure durations are appropriate for assessing the human health risk. Table 4.3.2.1 provides a summary of the representative results from experimental toxicology studies with TCVP.

Table 4.3.2.1 – TCVP BMD_{10} Results (mg/kg/day) for RBC and Brain AChE Inhibition Over Time in Adult Rats

MRID (study)	Days of Dosing	% inhibition at LOAEL (mg/kg) or the BMD_{10} [1]	
		RBC	
		Males	Females
MRID 48773401a	1 day	10% at 6.5 (BMD_{10})	10% at 14.9 (BMD_{10})
MRID 48773401 (repeat CCA)	11 days	10% at 7.7 (BMD_{10})	10% at 8.7 (BMD_{10})
MRID 45570601 (21-day oral)	21 days	No inhibition	10% at 9.9 (BMD_{10})
MRID 43371201 (90-day oral)	90 days	10% at 61.6 (BMD_{10})	10% at 10.5 (BMD_{10})
MRID 42980901 (chronic oral)	365 days	No inhibition	29% at 63
		Brain	

Table 4.3.2.1 – TCVP BMD_{10} Results (mg/kg/day) for RBC and Brain AChE Inhibition Over Time in Adult Rats			
MRID (study)	**Days of Dosing**	**% inhibition at LOAEL (mg/kg) or the BMD_{10} [1]**	
		Males	**Females**
MRID 48773401a	1 day	10% at 7.4 (BMD_{10})	10% at 11.6 (BMD_{10})
MRID 48294601 (acute CCA)	1 day	10% at 6.8 (BMD_{10})	10% at 11.3 (BMD_{10})
MRID 48773401 (repeat CCA)	11 days	10% at 33.8 (BMD_{10})	10% at 7.2 (BMD_{10})
MRID 45570601 (21-day oral)	21 days	No inhibition	10% at 14.7 (BMD_{10})
MRID 43371201 (90-day oral)	90 days	No inhibition	12% at 6.7
MRID 42980901 (chronic oral)	365 days	No inhibition	14% at 63

[1]The BMD, not the BMDL, estimates are shown when available in Table 4.3.2.1. According to the BMD guidance, the central estimate (i.e., the BMD) is used for purposes of comparison. The LOAEL and percent inhibition is presented when a BMD estimate is not available.

In adults, OPs generally exhibit a phenomenon known as steady state cholinesterase (AChE) inhibition. After repeated dosing at the same dose, the degree of inhibition comes into equilibrium with the production of new, uninhibited enzyme. At this point, the amount of AChE inhibition at a given dose remains consistent across duration. In general, OPs reach steady state within 2-3 weeks; a pattern that is observed for most OPs, but not every OP, like TCVP, which shows no difference in response across duration. For TCVP, the results in Table 4.3.2.1 show a similar response across durations suggesting that steady state is reached after a single day of exposure. Further, TCVP exhibits a shallow dose-response curve for cholinesterase inhibition; *i.e.*, large increases in administered dose result in only small changes in AChE inhibition, although this may be attributed to differences in time after dosing that the cholinesterase measurements were made. This shallow dose response leads to variability in the AChE data and a relatively broad range of values of3.2 to 61.6 mg/kg/day for BMD_{10}s and 2.8 to 26.3 mg/kg/day for $BMDL_{10}$s (Appendix B). Given the results in Table 4.3.2.1 for TCVP, single day and steady state durations should have the same point of departure for human health risk assessment. As such, the endpoint selection for TCVP considers data available for all durations of dosing when choosing a protective POD.

4.4 Literature Review on Neurodevelopment Effects

For the OPs, historically the agency has used inhibition of AChE as the POD for human health risk assessment; at present time, this policy continues. This science policy is based on decades of work which shows that AChE inhibition is the initial event in the pathway to acute cholinergic neurotoxicity. The use of AChE inhibition data for deriving PODs was supported by the FIFRA SAP (2008, 2012) for chlorpyrifos as the most robust source of dose-response data for extrapolating risk and is the source of data for PODs for TCVP. A detailed review of the epidemiological studies used in this review can be found either in the 2014 chlorpyrifos revised

draft human health risk assessment ((D424485, D. Drew et al., 12/29/2014) or in the 2015 literature review for other organophosphates (OPP/USEPA; D331251; 9/15/15).

Newer lines of research on OPs in the areas of potential AOPs, *in vivo* animal studies, and notably epidemiological studies in mothers and children, have raised some uncertainty about the agency's risk assessment approach with regard to the potential for neurodevelopmental effects in fetuses and children. Many of these studies have been the subject of review by the agency over the last several years as part of efforts to develop a risk assessment for chlorpyrifos (D424485, D. Drew et al., 12/29/2014). Initially, the agency focused on studies from three US cohorts: 1) The Mothers and Newborn Study of North Manhattan and South Bronx performed by the Columbia Children's Center for Environmental Health (CCCEH) at Columbia University; 2) the Mt. Sinai Inner-City Toxicants, Child Growth and Development Study or the "Mt. Sinai Child Growth and Development Study;" and 3) the Center for Health Assessment of Mothers and Children of Salinas Valley (CHAMACOS) conducted by researchers at University of California Berkeley. The agency has evaluated these studies and sought external peer review (FIFRA SAP reviews in 2008 and 2012; federal panel, 2013[8]) and concludes they are of high quality. In the three US epidemiology cohort studies, mother-infant pairs were recruited for the purpose of studying the potential health effects of environmental exposures during pregnancy on subsequent child development. Each of these cohorts evaluated the association between prenatal chlorpyrifos and/or OP exposure (with adverse neurodevelopmental outcomes in children through age 7 years. For the 2014 chlorpyrifos revised human health risk assessment (D424485, D. Drew et al., 12/29/2014), EPA included epidemiologic research results from these three US prospective birth cohort studies but primarily focused on the results of CCCEH since this cohort has published studies on the association between cord blood levels of chlorpyrifos and neurodevelopmental outcomes. The agency retained the FQPA 10X Safety Factor (SF) in the 2014 chlorpyrifos revised risk assessment, in large part, based on the findings of these studies.

In the 2015 updated literature review (OPP/USEPA; D331251; 9/15/15), the agency conducted a systematic review expanding the scope of the 2012/2014 review focused on US cohort studies with particular emphasis on chlorpyrifos. The expanded 2015 review includes consideration of the epidemiological data on any OP pesticide, study designs beyond prospective cohort studies, and non-U.S. based studies. The updated literature review identified seven studies which were relevant (Bouchard et al., 2010; Fortenberry et al., 2014; Furlong et al., 2014; Guodong et al., 2012; Oulhote and Bouchard, 2013; Zhang et al., 2014; Shelton et al., 2014). These seven studies have been evaluated in context with studies from the 2012/2014 review (D424485, D. Drew et al., 12/29/2014). Only a brief summary is provided below.

The OP exposure being assessed in many of these studies used concentrations of urinary dialkyl phosphate metabolites (DAPs) as the urinary biomarker. Total DAPs is a non-specific measure of OP exposure and is the sum of six separate molecules - three dimethyl alkylphosphate (DMAP) molecules of DMP, DMTP, DMDTP, and three diethyl alkylphosphate (DEAP)

[8] http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2008-0850-0170

molecules of DEP, DETP, and DEDTP. Each metabolite is a breakdown product from multiple OPs (Table 4.4.-1; CDC, 2008)[9]. Specifically, DMP, DMTP, and DMDTP are associated with 18, 13, and 5 OPs, whereas DEP, DETP, and DEDTP are associated with 10, 10, and 4 OPs, respectively. Thus, using urinary DAPs alone as an exposure measure, it is not possible to separate the exposure and associated effects for single, specific OPs.

Table 4.4.1. CDC Table of organophosphate pesticides and their dialkyl phosphate metabolites (2008).

Pesticide	DMP	DMTP	DMDTP	DEP	DETP	DEDTP
Azinphos methyl	X	X	X			
Chlorethoxyphos				X	X	
Chlorpyrifos				X	X	
Chlorpyrifos methyl	X	X				
Coumaphos				X	X	
Dichlorvos (DDVP)	X					
Diazinon				X	X	
Dicrotophos	X					
Dimethoate	X	X	X			
Disulfoton				X	X	X
Ethion				X	X	X
Fenitrothion	X	X				
Fenthion	X	X				
Isazaphos-methyl	X	X				
Malathion	X	X	X			
Methidathion	X	X	X			
Methyl parathion	X	X				
Naled	X					
Oxydemeton-methyl	X	X				
Parathion				X	X	
Phorate				X	X	X
Phosmet	X	X	X			
Pirimiphos-methyl	X	X				
Sulfotepp				X	X	
Temephos	X	X				
Terbufos				X	X	X
Tetrachlorvinphos	X					
Trichlorfon	X					

DMP = dimethylphosphate; DEP = diethylphosphate; DMTP = dimethylthiophosphate; DMDTP = dimethyldithiophosphate; DETP = diethylthiophosphate; DEDTP = diethyldithiophosphate.

[9] http://www.cdc.gov/nchs/data/nhanes/nhanes_03_04/l26opd_c_met_organophosphorus_pesticides.pdf

For studies which measured urinary 3,5,6-trichloro-2-pyridinol (TCPy) (e.g., Fortenberry et al., 2014; Eskenazi et al., 2007; Whyatt et al., 2009), this metabolite can be derived from chlorpyrifos, chlorpyrifos-methyl, and the herbicide triclopyr. TCPy is also the primary environmental degradate of chlorpyrifos, chlorpyrifos-methyl, and triclopyr; thus exposure can be found directly on food treated with these pesticides. CCCEH studies have largely used chlorpyrifos measured in cord blood as the specific biomarker (e.g., Lovasi et al., 2010; Whyatt et al., 2004; Rauh et al., 2011). The CHARGE study (Shelton et al., 2015) did not measure biomarkers but instead used geospatial analysis to focus on the residential proximity to OP exposure using data from the California Department of Pesticide Regulation, with five OPs accounting for a total of 73% of the pesticide applied near residential settings (chlorpyrifos, acephate, diazinon, bensulide, and dimethoate).

Similarly, DAPs can be found directly on food following OP applications (Zhang et al., 2008; Chen et al., 2012). Specifically, studies have shown that DAPs may form as environmental degradates from abiotic hydrolysis, photolysis, and plant metabolism (Zhang et al., 2008; Chen et al., 2012; Racke et al., 1994). Furthermore, since these DAPs are excreted more rapidly and extensively than the parent OPs (Zhang et al., 2008; Forsberg et al., 2008), direct exposure to DAPs may lead to an overestimate of OP exposure when using urinary DAPs as a biomarker of OP exposure. The agency recognizes that this is a source of uncertainty when using DAPs for assessing OP exposure and will continue to monitor this issue in future assessments.

With respect to neurological effects near birth, the CHAMACOS and Mt. Sinai cohorts measured neurological effects at birth, and observed a putative association with total DEAP, total DMAP, and total DAP exposure (Engel et al., 2007; Young et al., 2005). Similarly, a Chinese study (Zhang et al., 2014) reported statistically significant associations for total DEAPs, total DMAPs, and total DAPs from prenatal OP pesticide exposure and neonatal neurodevelopment assessed 3 days after birth. However, another cross-sectional Chinese study, Guodong et al. (2012), observed no association with urinary DAPs and a developmental quotient score for 23-25 month old children.

The 3 US cohorts (CCCEH, Mt. Sinai, CHAMACOS) each reported evidence of impaired mental and psychomotor development, albeit not consistent by age at time of testing (ranging from 6 month to 36 months across the three cohorts). Attentional problems and Attention Deficit Hyperactivity Disorder (ADHD) were reported by three prospective cohorts [Rauh et al., 2006; Eskenazi et al., 2007; Marks et al., 2010; and Fortenberry et al. (2014)] with additional support from a cross-sectional study, Bouchard et al. (2010). The exposure metric varied among these studies. Specifically, Fortenberry et al. (2014) found suggestive evidence of an association with TCPy and ADHD in boys, whereas statistically significant associations were observed by Rauh et al. (2006) with chlorpyrifos exposure and ADHD. Eskenazi et al. (2007) reported associations with total DMAPs and total DAPs and ADHD; Marks et al. (2010) reported associations with total DEAP, DMAP, and total DAP exposure and ADHD. In a national cross-sectional study of Canadian children, using 2007-2009 data for children age 6-11 years (Oulhote and Bouchard, 2013), there were no overall statistically significant associations observed between child urinary DEAP, DMAP, or total DAP metabolite levels and parentally reported behavioral problems. In

contrast, Bouchard et al. (2010), looking at U.S. children age 8-15 years in the 2000-2004 National Health and Nutrition Examination Survey (NHANES), observed a positive association between attention and behavior problems and total DAPs and DMAPs, but not DEAPs. As part of their analysis, Oulhote and Bouchard (2013) noted that their outcome assessment for behavioral problems may not have been as sensitive as Bouchard et al. (2010), which may in part account for the difference in the observed results from these studies.

In addition, the three US cohorts and the CHARGE study have reported suggestive or positive associations between OP exposure and autism spectrum disorders (Rauh et al., 2006; Shelton et al., 2014; Eskenazi et al., 2007; Furlong et al., 2014). Specifically, Furlong et al. (2014) documented suggestive evidence of an association between total DEAP exposure and reciprocal social responsiveness among blacks and boys. Eskenazi et al. (2007) reported a statistically significant association between pervasive developmental disorder (PDD) and total DAP exposure, whereas Eskenazi et al. (2010) reported non-significant, but suggestive, increased odds of PDD of 2.0 (0.8 to 5.1; p=0.14). Rauh et al. (2006) documented a significant association between PDD and specifically chlorpyrifos exposure. Both PDD and reciprocal social responsiveness are related to the autism spectrum disorder. Using a different exposure assessment method (geospatial analysis and residential proximity to total OP exposure), Shelton et al. (2014) also showed statistically significant associations between total OP exposure and ASD. While these studies vary in the magnitude of the overall strength of association, they have consistently observed a positive association between OP exposure and ASD. Finally, CCCEH, Mt. Sinai, CHAMACOS have reported an inverse relation between the respective prenatal measures of chlorpyrifos and intelligence measures at age 7 years (Rauh et al. ,2011; Engel et al., 2011; Bouchard et al., 2011).

Across the epidemiology database of studies, the maternal urine, cord blood, and other (meconium) measures provide evidence that exposure did occur to the fetus during gestation but the actual level of such exposure during the critical window(s) of susceptibility is not known. While significant uncertainties remain about the actual exposure levels experienced by mothers and infant participants in the children's health cohorts, it is unlikely that these exposures resulted in AChE inhibition. As part of the CHAMACOS study, Eskenazi et al. (2004) measured AChE activity and showed that no differences in AChE activity were observed. The biomarker data (chlorpyrifos) from the Columbia University studies are supported by the agency's dose reconstruction analysis using the Physiologically Based Pharmacokinetic and Pharmacodynamic (PBPK-PD) model (D424485, D. Drew et al., 12/29/2014). Following the recommendation of the FIFRA SAP (2012), the agency conducted a dose reconstruction analysis of residential uses available prior to 2000 for pregnant women and young children inside the home. The PBPK-PD model results indicate for the highest exposure considered (i.e., indoor broadcast use of a 1% chlorpyrifos formulation) <1% RBC AChE inhibition was produced in pregnant women. While uncertainty exists as to actual OP exposure at (unknown) critical windows of exposure, EPA believes it is unlikely individuals in the epidemiology studies experienced RBC AChE inhibition.

A review of the scientific literature on potential modes of action/adverse outcome pathways (MOA/AOP)[10] leading to effects on the developing brain was conducted for the 2012 FIFRA SAP meeting (USEPA, 2012) and updated for the December 2014 chlorpyrifos revised risk assessment (D424485, D. Drew et al., 12/29/2014). In short, multiple biologically plausible hypotheses and pathways are being pursued by researchers that include targets other than AChE inhibition, including cholinergic and non-cholinergic systems, signaling pathways, proteins, and others. However, no one pathway has sufficient data to be considered more credible than the others. The fact that there are, however, sparse AOP data to support the *in vitro* to *in vivo* extrapolation, or the extrapolation from biological perturbation to adverse consequence significantly limits their quantitative use in risk assessment. The SAP concurred with the agency in 2008 and 2012 about the lack of definable key events in a MOA/AOP leading to developmental neurobehavioral effects. However, since the 2014 literature review, there are no substantive changes in the ability to define and quantitate steps in an MOA/AOP leading from exposure to effects on the developing brain. Published and submitted guideline DNT laboratory animal studies have been reviewed for OPs as part of the 2012/2014 review (D424485, D. Drew et al., 12/29/2014) and the updated 2015 review (OPP/USEPA; D331251; 9/15/15). Neurobehavioral alterations in laboratory animals were often reported, albeit at AChE inhibiting doses, but there was generally a lack of consistency in terms of pattern, timing, or dose-response for these effects, and a number of studies were of lower quality. However, this information does provide evidence of long-lasting neurodevelopmental disorders in rats and mice following gestational exposure.

At this time, a MOA(s)/AOP(s) has/have not been established for neurodevelopmental outcomes. This growing body of literature does demonstrate, however, that OPs are biologically active on a number of processes that affect the developing brain. Moreover, there is a large body of *in vivo* laboratory studies which show long-term behavioral effects from early life exposure, albeit at doses which cause AChE inhibition. EPA considers the results of the toxicological studies relevant to the human population, as qualitatively supported by the results of epidemiology studies. The agency acknowledges the lack of established MOA/AOP pathway and uncertainties associated with the lack of ability to make strong causal linkages and unknown window(s) of susceptibility. These uncertainties do not undermine or reduce the confidence in the findings of the epidemiology studies. The epidemiology studies reviewed in the 2012/2014 and 2015 literature reviews represent different investigators, locations, points in time, exposure assessment procedures, and outcome measurements. Despite all these differences in study design, with the exception of two negative studies in the 2015 literature review (Guodong et al., 2012; Oulhote and Bouchard, 2013), authors have identified associations with neurodevelopmental outcomes associated with OP exposure across four cohorts and twelve study citations. Specifically, there is evidence of delays in mental development in infants (24-36 months), attention problems and autism spectrum disorder in early childhood, and intelligence decrements in school age children

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[10] Mode of action (MOA) and adverse outcome pathways (AOPs) describe a set of measureable key events that make up the biological processes leading to an adverse outcome and the causal linkages between such events.

who were exposed to OPs during gestation. Investigators reported strong measures of statistical association across several of these evaluations (odds ratios 2-4 fold increase in some instances), and observed evidence of exposures-response trends in some instances, *e.g.*, intelligence measures.

As section 408(b)(2)(C) of the Federal Food, Drug, and Cosmetic Act (FFDCA) instructs EPA, in making its "reasonable certainty of no harm" finding, that in "the case of threshold effects, an additional tenfold margin of safety for the pesticide chemical residue and other sources of exposure shall be applied for infants and children to take into account potential pre- and postnatal toxicity and completeness of data with respect to exposure and toxicity to infants and children." Section 408 (b)(2)(C) further states that "the Administrator may use a different margin of safety for the pesticide chemical residue only if, on the basis of reliable data, such margin will be safe for infants and children." Given the totality of the evidence, there is sufficient uncertainty in the human dose-response relationship for neurodevelopmental effects which prevents the agency from reducing or removing the statutory 10X FQPA Safety Factor. For the TCVP human health risk assessment, a value of 10X has been applied. Similarly, a database uncertainty factor of 10X will be retained for occupational risk assessments. The agency will continue to evaluate the epidemiology studies and pursue approaches for quantitative or semi-quantitative comparisons between doses which elicit AChE inhibition and those which are associated with neurodevelopmental outcomes prior to a revised human health risk assessment.

4.5 Safety Factor for Infants and Children (FQPA Safety Factor)

As noted above, the lack of an established MOA/AOP makes quantitative use of the epidemiology studies in risk assessment challenging, particularly with respect to determining dose-response, critical duration of exposure, and window(s) of susceptibility. However, exposure levels in the range measured in the epidemiology studies are likely low enough that they are unlikely to result in AChE inhibition. Epidemiology studies consistently identified associations with neurodevelopmental outcomes associated with OP exposure such as delays in mental development in infants (24-36 months), attention problems and autism spectrum disorder in early childhood, and intelligence decrements in school age children. Therefore, there is a need to protect children from exposures that may cause these effects; this need prevents the agency from reducing or removing the statutory FQPA Safety Factor. **Thus, the FQPA 10X Safety Factor will be retained for TCVP for the population subgroups that include infants, children, youths, and women of childbearing age for all exposure scenarios.** [11]

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[11] HED's standard toxicological, exposure, and risk assessment approaches are consistent with the requirements of EPA's children's environmental health policy (https://www.epa.gov/children/epas-policy-evaluating-risk-children).

4.5.1 Completeness of the Toxicology Database

The database of toxicology studies for TCVP is complete and includes developmental toxicity studies in the rat and rabbit, a reproductive toxicity study in the rat, acute and subchronic neurotoxicity studies in the rat, a developmental neurotoxicity study in the rat, a three component comparative cholinesterase study in the rat (acute, repeat, and gestational exposure), and an acute delayed hen neurotoxicity study.

As discussed in Section 4.5, there is uncertainty in the human dose-response relationship for neurodevelopmental effects and this warrants retention of the FQPA Safety Factor for the population subgroups that include infants, children, youths, and women of childbearing age for all exposure scenarios.

4.5.2 Evidence of Neurotoxicity

TCVP is an organophosphate insecticide with an established neurotoxic AOP; neurotoxicity is the most sensitive effect in all species, routes, and lifestages and is being used to derive points of departure (PODs). Neurotoxicity related to inhibition of AChE by TCVP, which was noted in the ACN and rabbit developmental toxicity studies, included transient clinical signs characteristic of cholinergic toxicity and tremors, as discussed above. The points of departure selected for this risk assessment are protective of these clinical signs.

4.5.3 Evidence of Sensitivity/Susceptibility in the Developing or Young Animal

The concern for susceptibility is low based on the lack of susceptibility following *in utero* exposure to TCVP in either the rat or rabbit developmental toxicity study or following *in utero* and/or pre-/post-natal exposure to TCVP in the 2-generation reproduction rat study. The apparent quantitative susceptibility observed in pups in the DNT occurred at the same dose level where 60% RBC and 45% brain cholinesterase inhibition occurred in pups and 62% RBC and 57% brain inhibition occurred in the adult females in the repeat CCA study. This comparison demonstrates that significant inhibition and toxicity also occurred in the maternal rat in the DNT, and repeat dosing showed no sensitivity with respect to the magnitude of the cholinesterase inhibition between the dam and pups. Furthermore, the effects observed in the DNT occurred at a dose 70-fold higher than the point of departure (POD). The POD is based on the AChE data from PND11 and PND21 pups from the acute CCA study, which provided the lowest POD, and is protective of the effects observed in the DNT.

As discussed in Section 4.5, there is uncertainty in the human dose-response relationship for neurodevelopmental effects and this warrants retention of the FQPA Safety Factor for the population subgroups that include infants, children, youths, and women of childbearing age for all exposure scenarios.

4.5.4 Residual Uncertainty in the Exposure Database

There are no residual uncertainties in the exposure database. The mostly refined dietary risk assessment uses food residues levels from monitoring data and from empirical studies, percent livestock treated data and model-estimated drinking water concentrations from maximum application rates. Residential exposure assessments use data from surrogate and chemical-specific sources. The exposure assumptions will not underestimate risks.

4.6 Toxicology Endpoint and Point of Departure Selections

4.6.1 Dose-Response Assessment

Table 4.6.4.1 summarizes the TCVP toxicity endpoints and points of departure (PODs) selected from an evaluation of the database. This endpoint selection was based on a weight of the evidence evaluation using the following considerations:

- *Relative sensitivity of the brain and RBC compartments*: For TCVP, there is no consistent pattern across studies, durations, lifestages, and routes. Following acute oral exposure, RBC and brain are equally affected, whereas the RBC compartment provided the lower BMDL estimate following repeat oral exposure in adults. Also, for each age group in the CCA studies, the magnitude of the RBC and brain inhibition is similar. Based upon the robustness of the AChE data and dose-response across the dose selection in the acute dose CCA rat study (see Appendix B for BMD analysis results), the RBC AChE data from PND 11 and 21 male and female pups were selected as the endpoint for deriving the acute and steady state POD for risk assessment.
- *Potentially susceptible populations (fetuses, juveniles, pregnant dams)*: The available AChE data across multiple lifestages (adults, pregnant females, fetuses, juveniles) show no quantitative sensitivity following repeat or acute exposure. The fetus is not more sensitive than the pregnant dam, and pregnant females were not more sensitive than non-pregnant females. There is also no consistent pattern with respect to sex difference. In the acute CCA, the adult male shows greater inhibition in both compartments than the adult female, whereas the adult female shows more inhibition (both compartments) in the repeat CCA and other repeat dose studies than the adult male.
- *Route of exposure:* It is preferred to match, to the degree possible, the route of exposure in the toxicity study with the exposure scenario(s) of interest. In the case of TCVP, there are single and repeat dose oral, repeat dose dermal, and repeat dose inhalation studies that contain measurements of RBC and brain AChE inhibition.
- *Duration of exposure:* It is preferred to match, to the degree possible, the duration of toxicity study with the exposure duration of interest. In the case of TCVP, there are single day and steady state/repeat exposure oral studies and steady state dermal and inhalation studies. The oral AChE data show the magnitude of AChE inhibition does not significantly increase with time such that AChE inhibition from a single oral exposure is comparable to AChE inhibition after repeated oral exposure.
- *Consistency across studies:* In cases where multiple datasets are available for a single duration, it is important to evaluate the extent to which data are consistent (or not) across

studies. Based on a weight of evidence approach, the TCVP database allows for PODs to be derived from the most conservative BMDLs, which are consistent for the PND 11 and PND 21 rats in the acute CCA and adult animals in the acute and repeat CCA thereby increasing the confidence in such values.

Consistent with risk assessments for other AChE-inhibiting compounds, OPP has used a benchmark response (BMR) level of 10% and has thus calculated BMD_{10}s and $BMDL_{10}$s. The BMD_{10} is the estimated dose where AChE is inhibited by 10% compared to background AChE activity. The $BMDL_{10}$ is the lower confidence bound on the BMD_{10} value. As a matter of science policy, the agency uses the BMDL, not the BMD, as the PoD (USEPA, 2012). All BMD/BMDL modeling was completed using USEPA BMD Software, version 2.4; an exponential model was used to fit the data. Descriptions of the primary toxicity studies used for selecting toxicity endpoints and points of departure for various exposure scenarios are presented in Appendix A of this document, which includes an additional acute CCA identified since the last risk assessment. Summary tables of BMD analyses can be found in Appendix B and the technical details of the analysis can be found in the BMD memo (J. Bever; TXR No. 0056970; D420286).

Acute Dietary (All Populations)

A POD for the acute dietary (all populations) exposure scenario was derived from the results of the high quality, well-conducted acute dose CCA study (MRID 448773401a) in juvenile rats. Numerous estimates informed the $BMDL_{10}$ of 2.8 mg/kg/day, which was associated with RBC AChE inhibition in PND11 and PND 21 male and female juvenile rats and was therefore selected as the POD for the acute dietary exposure scenario for all populations. The lowest corresponding BMD_{10} was 3.2 mg/kg/day. Data from the young rat from the acute CCA study are appropriate for acute POD derivation, since effects were observed after a single exposure and the endpoint is the most sensitive adverse response in all populations.

The FQPA SF (10X) will be retained for infants, children, youths, and women of childbearing age due to uncertainty in the human dose-response relationship for neurodevelopmental effects (see Section 4.5). The acute population adjusted dose (aPAD) for these lifestages is 0.0028 mg/kg/day (includes a total uncertainty factor of 1000X: 10X to account for interspecies extrapolation and 10X for intraspecies variation and the 10X FQPA SF). The only population subgroup for dietary exposure scenarios for which the FQPA SF is not retained is adults 50-99 years of age; therefore, the aPAD for this population subgroup is 0.028 mg/kg/day.

Steady-State Dietary (All Populations)

A POD for the steady-state dietary (all populations) exposure scenarios was derived from the same acute dose CCA study used for the acute dietary. A $BMDL_{10}$ of 2.8 mg/kg/day associated with RBC cholinesterase inhibition in male and female PND 11 and 21 rats was selected as a suitable POD for the steady-state dietary exposure scenario. The lowest corresponding BMD_{10} was 3.2 mg/kg/day. Although the steady state dietary endpoint was selected from an acute dose comparative cholinesterase study, the duration of this study is considered appropriate for this exposure scenario since AChE data across the TCVP database demonstrate that there is no

progression of AChE inhibition over exposure duration, and steady state inhibition occurs essentially after a single dose. A longer-term exposure does not result in a lower POD, as evidenced by the larger BMD_{10}s found for the repeat dose CCA data.

An uncertainty factor of 1000X (10X to account for interspecies extrapolation, 10X for intraspecies variation, and 10X for FQPA SF due to uncertainty in the human dose-response relationship for neurodevelopmental effects (see Section 4.5)) is applied to the $BMDL_{10}$ to obtain an ssPAD of 0.0028 mg/kg/day for exposure scenarios with infants, children, youth, and women of child-bearing age. The only population subgroup for which the FQPA SF is not retained is adults 50-99; therefore, the ssPAD for this population subgroup is 0.028 mg/kg/day.

Incidental Oral, Steady State

For the purpose of assessing potential risk associated with incidental oral exposure from steady state durations, OPP selected the same POD (2.8 mg/kg/day) and endpoint as selected above for dietary exposure.

A total uncertainty factor of 1000X is appropriate for incidental oral exposures (10X for interspecies extrapolation, 10X for intraspecies variation, and a 10X FQPA SF due to uncertainty in the human dose-response relationship for neurodevelopmental effects (see Section 4.5)). The Level of Concern (LOC) for incidental oral exposures is 1000.

Dermal, Steady State

No quantification of dermal non-cancer risk is required for TCVP since there were: (1) no treatment related effects (no clinical signs) at doses up to and including the limit dose of 1000 mg/kg/day in the dermal toxicity study; (2) both RBC and brain cholinesterase activity were assessed in the dermal study and neither compartment was affected at the limit dose; (3) there is no concern for quantitative susceptibility for juvenile or gestational lifestages based on results of the developmental, reproductive, or CCA toxicity studies.

Inhalation, Steady State

The steady state inhalation POD was selected from a 4-week inhalation toxicity study (MRID 48803501) in rats, based on an increase in RBC cholinesterase inhibition in both sexes. Females had slightly higher modeled values ($BMDL_{10}$ of 0.022 mg/L/day: BMD_{10} of 0.12 mg/L/day) than males. The duration of this study is considered appropriate for the steady state exposure scenario since steady state occurs within 21 days, as demonstrated for other OPs, and a longer-term exposure would not be expected to result in a lower POD. The methods and dosimetry equations described in the agency's reference concentration (RfC) guidance are suited for calculating human equivalent concentrations (HECs) based on the inhalation toxicity POD obtained in rats exposed for 6 hours/day for an average of 5.5 days/week. The regional deposited dose ratio (RDDR), which accounts for the particulate diameter (mass median aerodynamic diameter [MMAD] and geometric standard deviation [GSD] of aerosols) can be used to estimate the different dose fractions deposited along the respiratory tract surface areas. Thus, the RDDR can

be used to adjust an observed inhalation particulate exposure of an animal to the predicted inhalation exposure for a human. For the subchronic inhalation toxicity study with TCVP, an RDDR of 2.525 was estimated based on extrarespiratory effects (RBC cholinesterase inhibition) in Sprague Dawley rats (bodyweight = 267g). The MMAD and GSD of 2.57 and 3.785 µm, respectively, at 0.05 mg/L were used to derive the RDDR.

The HECs are summarized in Table 4.6.4.3, as well as human equivalent doses (HEDs) calculated for residential and occupational handler scenarios. The standard interspecies extrapolation uncertainty factor can be reduced from 10X to 3X due to the HEC calculation accounting for pharmacokinetic (not pharmacodynamic) interspecies differences. The intraspecies uncertainty factor remains at 10X.

A total uncertainty factor of 300X is appropriate for inhalation exposures (3X for interspecies extrapolation, 10X for intraspecies variation, and a 10X FQPA SF for residential assessments or a 10X database uncertainty factor in occupational assessments due to uncertainty in the human dose-response relationship for neurodevelopmental effects (see Section 4.5)).

4.6.2 Recommendations for Combining Routes of Exposure for Risk Assessment

When there are potential occupational and residential exposures to a pesticide, the risk assessment must address exposures from three major routes (oral, dermal, and inhalation) and determine whether the individual exposures can be combined if they have the same toxicological effects. PODs for the oral, dermal, and inhalation routes are all derived from RBC cholinesterase inhibition. Thus, all routes can be combined.

4.6.3 Cancer Classification and Risk Assessment Recommendation

TCVP is classified as a Group C, possible human carcinogen, based on statistically significant increases in combined hepatocellular adenoma/carcinoma (primarily carcinomas) in the female B6C3F1 mouse, suggestive evidence of thyroid c-cell adenomas, and adrenal pheochromocytomas in the rat, as well as mutagenicity concerns. Following a reassessment of the mutagenicity data available on TCVP, it was determined that the relevance of the mutagenic findings to the tumorigenic response seen in female mice cannot be established. Therefore, a follow-up mouse micronucleus assay (OPPTS Harmonized Guideline 870.5395) is required for TCVP. Additionally, a study that investigates possible genotoxic activity in the target organ (liver) is required. This study should examine DNA damage potential (Comet assay, DNA adduct formation, or any other DNA target)[12]. A cancer potency factor (Q_1^*) of 1.83×10^{-3} $(mg/kg/day)^{-1}$ was estimated using the Weibull 83 time-to-tumor model. A 3/4 body weight scaling factor was used to convert from mouse to human equivalents. Following the submission and review of the required assays, the need for an updated cancer assessment will be determined.

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[12] N. McCarroll and D. Davis, 12/21/2016, Tetrachlorovinphos (TCVP): Revisit of Mutagenicity Studies, TXR#0057553, D437226.

4.6.4 Summary of Points of Departure and Toxicity Endpoints Used in Human Risk Assessment

See Tables 4.6.4.1, 4.6.4.2, and 4.6.4.3 below.

Table 4.6.4.1. Summary of Toxicological Doses and Endpoints for TCVP for Use in Dietary and Non-Occupational Human Health Risk Assessments

Exposure/ Scenario	Point of Departure	Uncertainty Factors*	Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary (all populations, except adults 50-99)	$BMDL_{10}$ = 2.8 mg/kg/day	UF_A= 10x UF_H=10x FQPA SF = 10x	Acute RfD = 0.028 mg/kg/day aPAD = 0.0028 mg/kg/day	Acute dose CCA study (MRID 48773401a) – Rat BMD_{10} = 3.2 mg/kg/day, based on PND11 and 21 male and female RBC AChE inhibition
Acute Dietary (Adults 50-99)	$BMDL_{10}$ = 2.8 mg/kg/day	UF_A= 10x UF_H=10x FQPA SF = 1x	Acute RfD = 0.028 mg/kg/day aPAD = 0.028 mg/kg/day	Acute dose CCA study (MRID 48773401a) - Rat BMD_{10} = 3.2 mg/kg/day, based on PND 11 and 21 male and female RBC AChE inhibition
Steady State Dietary (all populations, except adults 50-99)	$BMDL_{10}$ = 2.8 mg/kg/day	UF_A= 10x UF_H=10x FQPA SF = 10x	Steady State RfD = 0.028 mg/kg/day ssPAD = 0.0028 mg/kg/day	Acute dose CCA study (MRID 48773401a) – Rat BMD_{10} = 3.2 mg/kg/day, based on PND 11 and 21 male and female RBC AChE inhibition
Steady State Dietary (Adults 50-99)	$BMDL_{10}$ = 2.8 mg/kg/day	UF_A= 10x UF_H=10x FQPA SF = 1x	Steady State RfD = 0.028 mg/kg/day ssPAD = 0.028 mg/kg/day	Acute dose CCA study (MRID 48773401a) - Rat BMD_{10} = 3.2 mg/kg/day, based on PND 11 and 21 male and female RBC AChE inhibition
Incidental Oral (steady state)	$BMDL_{10}$ = 2.8 mg/kg/day	UF_A= 10x UF_H=10x FQPA SF = 10x	Residential LOC for MOE = 1000	Acute dose CCA study (MRID 48773401a) - Rat BMD_{10} = 3.2 mg/kg/day, based on PND 11 and 21 male and female RBC AChE inhibition
Dermal (steady state)	No potential hazard *via* the dermal route, based on the lack of treatment-related effects, including the lack of RBC and brain cholinesterase inhibition following repeat dermal exposure of rats at dose levels up to 1000 mg/kg/day and no concern for quantitative susceptibility.			

Inhalation (steady state)	$BMDL_{10}$=0.022 mg/L/day (males)	UF_A= 3x UF_H=10x FQPA SF = 10X	Residential LOC for MOE = 300	Subchronic Inhalation Toxicity Study (MRID 48803501) – Rat BMD_{10} = 0.12 mg/L/day, based on RBC AChE inhibition in both sexes
Cancer (oral, dermal, inhalation)	Classification: A possible human (Group C) carcinogen. Q_1* = 1.83 x 10^{-3} (mg/kg/day)$^{-1}$			

[1] **Explanation of Abbreviations:** Point of Departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no observed adverse effect level. LOAEL = lowest observed adverse effect level. UF = uncertainty factor. UF_A = extrapolation from animal to human (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies); MOE = margin of exposure. LOC = level of concern. RBC = red blood cell. AChE = acetylcholinesterase. $BMDL_{10}$= benchmark dose lower limit for 10% response. PAD = population adjusted dose. (a = acute. ss = steady state or maximal AChE inhibition.
*The 10X FQPA SF is retained for infants, children, youths, and women of childbearing age for all exposure scenarios due to uncertainty in the human dose-response relationship for neurodevelopmental effects (see Section 4.5). This includes all exposure scenarios, except the dietary exposure scenarios for the population subgroup adults 50-99 for which the FQPA SF has been reduced to 1X.

Table 4.6.4.2 Summary of Toxicological Doses and Endpoints for TCVP for Use in Occupational Human Health Risk Assessments

Exposure/ Scenario	Point of Departure	Uncertainty Factors	Level of Concern for Risk Assessment	Study and Toxicological Effects
Dermal (steady state)	No potential hazard *via* the dermal route, based on the lack of treatment-related effects, including the lack of RBC and brain cholinesterase inhibition following repeat dermal exposure of rats at dose levels up to 1000 mg/kg/day and no concern for quantitative susceptibility.			
Inhalation (steady state)	$BMDL_{10}$=0.022 mg/L/day (males)	UF_A= 3x UF_H=10x UF_{DB}= $10x^A$	Occupational LOC for MOE = 300	Subchronic Inhalation Toxicity Study (MRID 48803501) - Rat BMD_{10} = 0.12 mg/L/day, based on RBC AChE inhibition in both sexes
Cancer (oral, dermal, inhalation)	Classification: A possible human (Group C) carcinogen. Q_1* = 1.83 x 10^{-3} (mg/kg/day)$^{-1}$			

[1] **Explanation of Abbreviations:** Point of Departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no observed adverse effect level. LOAEL = lowest observed adverse effect level. UF = uncertainty factor. UFA = extrapolation from animal to human (interspecies). UFH = potential variation in sensitivity among members of the human population (intraspecies); UF_{DB} = database uncertainty factor; MOE = margin of exposure. LOC = level of concern. RBC = red blood cell. $BMDL_{10}$= benchmark dose lower limit for 10% response. AChE = acetylcholinesterase. SS = steady state or maximal AChE inhibition which occurs around 2-3 weeks for OPs and is a specific exposure assessment conducted

for OPs instead of the traditional short, intermediate, or chronic assessments. The SS assessment is protective of longer durations including chronic.

[A] The 10X database uncertainty factor applies to occupational worker assessment to account for potentially pregnant workers due to uncertainty in the human dose-response relationship for neurodevelopmental effects (see Section 4.5).

Table 4.6.4.3 Summary of HEC/HED Values for TCVP

Population	Scenario	Tox Duration Adjustment		HEC		HED
		hours/day[a]	days/week[b]	mg/L	mg/m^3	mg/kg/day
Occupational	Handler	0.75	1	0.042	41.663	3.94
Residential	Handler			0.056	55.550	1.31
	Bystander	0.25	0.714	0.010	9.920	

HEC = human-equivalent concentration; HED = human-equivalent dose. See Appendix C for details.
HEC = rat POD × daily duration adjustment × weekly daily duration adjustment × RDDR.
HED = HEC × human-specific conversion factor (11.8 L/hr/kg) × daily duration.
[a] hours of exposure [animal study (6 hours) ÷ human worker (8 hours) or bystander (24 hours)]
[b] days of exposure [animal study (5 days/week ÷ bystander (7 days/week)/human worker (5 days/week)]

4.7 Endocrine Disruption

As required by FIFRA and FFDCA, EPA reviews numerous studies to assess potential adverse outcomes from exposure to chemicals. Collectively, these studies include acute, subchronic and chronic toxicity, including assessments of carcinogenicity, neurotoxicity, developmental, reproductive, and general or systemic toxicity. These studies include endpoints which may be susceptible to endocrine influence, including effects on endocrine target organ histopathology, organ weights, estrus cyclicity, sexual maturation, fertility, pregnancy rates, reproductive loss, and sex ratios in offspring. For ecological hazard assessments, EPA evaluates acute tests and chronic studies that assess growth, developmental and reproductive effects in different taxonomic groups. As part of its reregistration decision for TCVP, EPA reviewed these data and selected the most sensitive endpoints for relevant risk assessment scenarios from the existing hazard database. However, as required by FFDCA section 408(p), TCVP is subject to the endocrine screening part of the Endocrine Disruptor Screening Program (EDSP).

EPA has developed the EDSP to determine whether certain substances (including pesticide active and other ingredients) may have an effect in humans or wildlife similar to an effect produced by a "naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." The EDSP employs a two-tiered approach to making the statutorily required determinations. Tier 1 consists of a battery of 11 screening assays to identify the potential of a chemical substance to interact with the estrogen, androgen, or thyroid (E, A, or T) hormonal systems. Chemicals that go through Tier 1 screening and are found to have the potential to interact with E, A, or T hormonal systems will proceed to the next stage of the EDSP where EPA will determine which, if any, of the Tier 2 tests are necessary based on the available data. Tier 2 testing is designed to identify any adverse endocrine-related effects caused by the substance, and establish a dose-response relationship between the dose and the E, A, or T effect.

Under FFDCA section 408(p), the agency must screen all pesticide chemicals. Between October 2009 and February 2010, EPA issued test orders/data call-ins for the first group of 67 chemicals, which contains 58 pesticide active ingredients and 9 inert ingredients. A second list of chemicals identified for EDSP screening was published on June 14, 2013[13] and includes some pesticides scheduled for registration review and chemicals found in water. Neither of these lists should be construed as a list of known or likely endocrine disruptors. TCVP is on List 1 for which EPA has received all the required Tier 1 assay data. The agency has reviewed all of the assay data received for the appropriate List 1 chemicals and the conclusions of those reviews are available in the chemical-specific public dockets. For further information on the status of the EDSP, the policies and procedures, the lists of chemicals, future lists, the test guidelines and the Tier 1 screening battery, please visit our website[14].

5.0 Dietary Exposure and Risk Assessment

5.1 Metabolite/Degradate Residue Profile

5.1.1 Summary of Plant and Animal Metabolism Studies

Residue Chemistry Memo: DP# 243528, 3/11/98, D. Miller
Residue Chemistry Memo: DP# 206721, 9/21/94, D. Miller (Addendum to RED)
Residue Chemistry Chapter to Tetrachlorvinphos RED (DP# 199644, 7/6/94, F. Suhre)
Residue Chemistry Memo: J. Abbotts, No DP#, 4/93, Results of Metabolism Committee Meeting

There are no registrations or tolerances for plant commodities, so plant metabolism studies are not required for TCVP. The qualitative nature of the residue in ruminants following oral or dermal dosing, and in poultry following dermal application, is adequately understood based on previously submitted studies. The HED Metabolism Committee (9/8/93 Meeting) has determined that the residues of concern for tolerance enforcement and for risk assessment for carcinogenicity are the parent compound and four metabolites: tetrachlorvinphos, des-O-methyl tetrachlorvinphos, 1-(2,4,5-trichlorophenyl)ethanol (free and conjugated forms), 2,4,5-trichloroacetophenone, and 1-(2,4,5-trichlorophenyl)ethanediol. For the non-cancer risk assessment for cholinesterase inhibition, tetrachlorvinphos is the only residue of concern.

5.1.2 Summary of Environmental Degradation

Drinking Water Assessment Memo (EFED): DP# 419448, 11/6/14, C. Peck[15]

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[13] See http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2009-0477-0074 for the final second list of chemicals.

[14] http://www.epa.gov/endo/

[15] C. Peck, 11/6/2014, D419448, Tetrachlorvinphos (TCVP) Drinking Water Assessment for Registration Review

TCVP is moderately mobile in soil and not stable in terrestrial or aquatic environments. The TCVP degradates appear to be as mobile, and in most cases more mobile, than the parent. TCVP is soluble in water at up to 11.6 mg/L, and is not expected to volatilize significantly due to a low vapor pressure of 2.6×10^{-7} torr (25°C). The compound is hydrophobic (Log K_{ow} of 3.53). TCVP hydrolyzes in water at a pH-dependent rate. Hydrolysis is relatively rapid in alkaline water (half-life of 10.3 days at pH 9). In neutral to acidic water (pH 5 to 7), TCVP hydrolyzes with slower half-lives of 30 to 57 days. A major degradate of hydrolysis found in the aqueous solution at pH 9 was des-O-methyl tetrachlorvinphos (28% at Day 21). Hydrolysis rates for the TCVP Total Residue of Concern (TRC) could not be calculated, as not all degradates in the study extracts were identified; therefore, TCVP TRC was considered stable to hydrolysis.

TCVP isomer mixture (50:50, Z:E) readily biodegraded in aerobic soils, with a half-life of approximately 9 days. However, the rate of biodegradation for the mixed isomer of the parent TCVP was slightly reduced as concentrations decreased, which may indicate that one isomer degrades more rapidly than the other. Major soil degradates include TCPEol, TCCEol, TCPEone and TCBA. The TCVP TRC that were identified in the aerobic soils biodegraded with half-lives of from 53 to 200 days.

5.1.3 Comparison of Metabolic Pathways

Metabolism in ruminants (dermal and oral administration; tissue), poultry (oral; tissue) and rats (oral; excreta) is similar, generally resulting in parent TCVP and the four metabolites of concern (TCVPdeme, TCPEdiol, TCPEone and TCPEol). However, the metabolite TCPEone was not found in detectable levels in the rat metabolism study and the metabolite TCPEdiol was not detected in the goat studies. Unchanged parent TCVP was found in the goat dermal study, but was not detected in the goat oral study.

5.1.4 Residues of Concern Summary and Rationale

The HED Metabolism Committee (9/8/93 Meeting) has determined that the total residues of concern (TRC) for carcinogenicity are the parent compound tetrachlorvinphos and metabolites which, like tetrachlorvinphos, contain the 2,4,5 trichlorobenzene ring. For livestock commodities, the total residues of concern for carcinogenicity are tetrachlorvinphos [TCVP] plus the following four metabolites: des-O-methyl tetrachlorvinphos [TCVPdeme]; 1-(2,4,5-trichlorophenyl)ethanol (free and conjugated forms) [TCPEol]; 2,4,5-trichloroacetophenone [TCPEone]; and 1-(2,4,5-trichlorophenyl)ethanediol [TCPEdiol]. For drinking water carcinogenicity assessment, the total residues of concern include the four aforementioned metabolites for livestock plus 2 additional degradates: l-(2,4,5-trichlorophenyl)-2-chloroethanol [TCCEol], and 2,4,5-trichlorobenzoic acid [TCBA].

For the non-cancer risk assessment for cholinesterase inhibition, TCVP is the only residue of concern. For tolerance enforcement the residues of concern include TCVP plus, TCVPdeme, TCPEdiol, TCPEone and TCPEol.

See Appendix E for a table of parent and metabolite structures and chemical properties.

Table 5.1.4 Summary of Metabolites and Degradates to be included in the Risk Assessment and Tolerance Expression				
Matrix		**Residues included in Risk Assessment (Cholinesterase Inhibition)**	**Residues included in Risk Assessment (Carcinogenicity)**	**Residues included in Tolerance Expression**
Plants	Primary Crop	NA	NA	NA
	Rotational Crop	NA	NA	NA
Livestock	Ruminant	TCVP	TCVP, TCVPdeme, TCPEdiol, TCPEone and TCPEol	TCVP, TCVPdeme, TCPEdiol, TCPEone and TCPEol
	Poultry	TCVP	TCVP, TCVPdeme, TCPEdiol, TCPEone and TCPEol	TCVP, TCVPdeme, TCPEdiol, TCPEone and TCPEol
Drinking Water		TCVP	TCVP, TCVPdeme, TCPEdiol, TCPEone and TCPEol, TCCEol, TCBA	NA

NA= not applicable
TCVP= tetrachlorvinphos
TCVPdeme,= des-O-methyl tetrachlorvinphos
TCPEol= 1-(2,4,5-trichlorophenyl)ethanol (free and conjugated forms)
TCPEone= 2,4,5-trichloroacetophenone
TCPEdiol= 1-(2,4,5-trichlorophenyl)ethanediol
TCCEol =l-(2,4,5-trichlorophenyl)-2-chloroethanol
TCBA =2,4,5-Trichlorobenzoic acid

5.2 Residue Chemistry and Food Residue Profile

Residue Chemistry Memo: D243528, 3/11/98, D. Miller

Residue Chemistry

Tolerances are established for residues of TCVP in animal commodities since residues may occur in milk, eggs, meat, fat, or meat byproducts as a result of the registered uses on livestock (oral and dermal uses) and around livestock premises. There are no registered uses on plant (including feedstuffs) commodities. This section provides the background and current status of residue chemistry requirements for TCVP and includes residue data submitted and reviewed since the 1994 Residue Chemistry Chapter of the TCVP RED and the 2006 TCVP RED.

The 1994 Residue Chemistry Chapter cited the need for the following magnitude of the residue studies: *New magnitude of the residue studies reflecting oral and dermal exposure of beef cattle, dairy cattle, and hogs, and dermal exposure of poultry to tetrachlorvinphos are required. All residues of concern should be analyzed in cattle, hogs, and poultry using validated analytical methods.*

Subsequent to the TCVP RED, in 2007, residue studies on cattle (dermal and oral treatments; MRID 47193001) and poultry (dermal treatment; MRID 47193001) were submitted, as was a companion storage stability study (MRID 47193001) and a residue analytical method (MRID 47369201). Those studies were reviewed under DP #s D320848, D320858, D320859, and D381350 (C. Olinger, 10/7/10, *Tetrachlorvinphos. Cattle Oral/Dermal and Poultry Dermal Studies. Summary of Residue Data Submitted in Support of Reregistration*). The submitted magnitude of the residue studies on cattle and poultry were determined to be inadequate, but upgradeable pending submission of supporting storage stability data. The companion storage stability study was determined to be unacceptable because of study design. Additional information was also requested regarding the maximum storage duration of all samples collected from both the cattle and poultry studies. In 2011, additional information (MRIDs 486378101 and 48319001) pertaining to the storage stability deficiencies was submitted and reviewed (C. Olinger, 3/25/11, D385359 and D386954, *Tetrachlorvinphos. Response to Comment on Storage Stability Residue Data Deficiencies)*. The poultry and cattle residue data (860.1480) deficiencies are now fulfilled and no further data are being required.

In response to the data requirement for a residue study in hogs, a waiver request was submitted and granted in 2011 (C. Olinger, 4/25/11, D320857, *Tetrachlorvinphos. Request for Waiver of a Swine Magnitude of Residue Study)*. It was determined that TCVP residues in swine tissues are not likely to be higher than the residues in ruminants and that ruminant data may be translated to swine. The conclusion was based on the poor oral and dermal absorption of TCVP in livestock and the fact that residence time in swine intestines is significantly shorter relative to that in a ruminant. No additional residue data (860.1480) on hogs are being required.

In response to a TCVP Generic Data Call-In (GDCI) issued 12/29/09, data were submitted evaluating TCVP metabolites using the FDA Multiresidue Methods Test guidelines in Pesticide Analytical Manual (PAM) Vol. I (MRID 48655201) and were reviewed 7/5/12 (D. Drew, D396833, *Tetrachlorvinphos (TCVP). Multiresidue Methods (MRM) Study of the Metabolites of TCVP*). The data requirement for MRM testing (860.1360) has been fulfilled.

The registrant submitted a proposed method SCR/006 for tolerance enforcement of livestock commodities that includes detection of TCVP and the metabolites TCVPdeme, TCPEol, TCPEone and TCPEdiol (MRID 47369201, 2007). The HED review (D320848, D320858, D320859, and D381350) determined that the method was adequate, but that an independent laboratory validation (ILV) trial remained outstanding. A Generic Data Call-In (GDCI) for an ILV was originally issued December 29, 2009. A different proposed method (Method 14020.6106) and an associated ILV study (Method 14020.6107) were subsequently submitted to the agency (MRID 49419301, 2015). Because the proposed Method 14020.6106 monitors only a single ion transition for each analyte, alternative confirmatory procedures are necessary; the previously submitted method SCR/006 (MRID 47369201) is considered acceptable as a confirmatory method. The analytical method test data for 14020.6106 are classified as scientifically acceptable for use as an analytical method for ruminant and poultry commodities.

Food Residue Profile

The available magnitude of the residue study for dairy cattle reflect a combination of two treatments: oral administration of tetrachlorvinphos for 29-31 days at actual rates of 1.51-1.55 and 4.63 g ai/750 kg BW per day (6.3-6.5x and 19.3x, respectively, the maximum registered rate of 0.24 g ai/750 kg BW for feed-through treatment) and dermal spray treatments on three occasions, at ~14 day intervals, at actual rates of 10.11 and 19.2-19.5 g ai per animal per dose (~0.5 and 1.0x, respectively, the maximum registered rate of 18.9 g ai/animal for direct animal spray treatment). At the combined treatment regime (6.5x dermal spray plus 1x oral treatment), the maximum total residues of concern (with the maximum residues of the parent in parentheses) were: 0.072 (0.036) ppm for milk, 0.078 (<0.01) ppm for cream, 0.158 (<0.01) ppm for liver, 0.278 (0.015) ppm for kidney, 0.272 (0.212) ppm for muscle, 0.842 (0.558) ppm for subcutaneous fat, and 0.747 (0.340) ppm for peritoneal fat.

The available magnitude of the residue study for poultry reflects 6-7 dermal spray treatments of laying hens with an EC formulation, made at two-week retreatment intervals, at 0.0908, 0.182, or 0.545 g ai/hen/application. These application rates, respectively, correspond to ~0.5x, 1.0x, or 2.9x the maximum registered direct spray treatment rate of 0.19 g ai/bird daily. At ~1.0x, the maximum total residues of concern (with the maximum residues of the parent in parentheses) were: 0.288 (0.026) ppm for egg, 0.517 (0.016) ppm for liver, 0.583 (0.022) ppm for kidney, 0.396 (0.082) ppm for muscle, 19.405 (6.030) ppm for skin with fat, and 1.298 (0.099) ppm for abdominal fat.

There were no detectable residues of parent TCVP in the most recent USDA PDP monitoring data for beef meat, liver, or fat, or for milk and cream; nor were there detectable residues in pork fat. There were no detectable residues in chicken meat or liver. There was one detectable residue in egg just above the method limit of detection (LOD; 742 samples). PDP did not analyze chicken fat or skin for TCVP. The TCVP metabolites of concern for cancer assessment were not measured by PDP.

5.3 Water Residue Profile

Drinking Water Assessment Memo (EFED): D419448, 11/6/14, C. Peck

The Surface Water Concentration Calculator (SWCC) computer model was used to generate surface water Estimated Drinking Water Concentrations (EDWCs) for use in the human health dietary risk assessment, while the PRZM-GW and SCI-GROW models were used to generate groundwater EDWCs. The residues of concern for acute and steady state dietary exposure included cholinesterase-inhibiting compounds, which were determined to be TCVP parent only. For carcinogenicity, (total) residues of concern (TRC) included TCVP and the following metabolites which, like TCVP, contain the 2,4,5 trichlorobenzene ring: des-O-methyl tetrachlorvinphos,1-(2,4,5-trichlorophenyl)ethanediol, TCPEol (1-(2,4,5-trichlorophenyl)ethanol), TCPEone (2,4,5-trichloroacetophenone), TCCEol (l-(2,4,5-trichlorophenyl)-2-chloroethanol), and TCBA (2,4,5-trichlorobenzoic acid).

Maximum EDWCs (based on maximum labeled usage for kennels, poultry droppings, garbage and manure piles, and corrals) for TCVP residues in surface water and groundwater for dietary assessment are presented in Table 5.3. Daily time series outputs for the thirty year simulation were also provided to HED for use in dietary exposure modeling.

This dietary assessment used the maximum total residues of concern (TRC) EDWC of 22.4 ug/L for the cancer analysis, input as a single point estimate. For the selected drinking water scenarios, a distribution of surface water residues was used probabilistically in the dietary model for non-cancer assessments based on cholinesterase inhibition. The following paragraph describes the derivation of those distributions.

Daily time-series outputs that simulate 29 years (1962-1990) of residues of TCVP in surface drinking water for the outdoor uses (on kennels, poultry droppings, garbage and manure piles, and corrals) were modeled using the SWCC. No further adjustments were made to the acute distribution files, but since the steady state average dietary assessments use 21-day forward rolling averages for drinking water, the steady state distributions were further adjusted to be 21-day forward rolling averages. In the 21-day rolling average distributions, the first data point is the average of days 1-21, the second data point is the average of days 2-22, the third data point is the average of days 3-23, etc. The 21-day rolling average continues until the last 20 days of residues of the final distribution year.

Table 5.3 Summary of Estimated Surface Water and Groundwater Concentrations for Tetrachlorvinphos

DRINKING WATER SOURCE (MODEL USED)	MAXIMUM ESTIMATED DRINKING WATER CONCENTRATION (EDWC)	
	Acute (µg/L) (TCVP only)	Cancer (µg/L) (TRC)
Surface water (SWCC)	**4.03**	4.11
Groundwater (PRZM-GW)	8.54×10^{-5}	**22.4**
Groundwater (SCI-GROW)	5.61×10^{-3}	7.36×10^{-2}

* EDWCs based on maximum labeled usage for kennels, poultry droppings, garbage and manure piles, and corrals.

5.4 Dietary Risk Assessment

Dietary Assessment Memo: D436835, 9/20/2016, D. Drew[16]

[16] D. Drew, 9/20/2016, Tetrachlorvinphos (TCVP). Revised Acute, Steady State, and Cancer Aggregate Dietary (Food and Drinking Water) Exposure and Risk Assessments for the Registration Review Human Health Risk Assessment, D436835.

The previous dietary risk assessment for tetrachlorvinphos was conducted on 10/29/2014 (D. Drew, D426985, *Tetrachlorvinphos (TCVP) Acute, Steady State, and Cancer Aggregate Dietary (Food and Drinking Water) Exposure and Risk Assessments for the Registration Review Human Health Risk Assessment*). That assessment has been updated in D436835 (D. Drew, 9/20/2016, Tetrachlorvinphos (TCVP). *Revised Acute, Steady State, and Cancer Aggregate Dietary (Food and Drinking Water) Exposure and Risk Assessments for the Registration Review Human Health Risk Assessment*) to reflect changes in the toxicological PODs for the acute and steady state dietary exposures. In addition, minor corrections have been made based on comments received on the 2014 dietary assessment (MRID 4989101, Bayer CropScience, *Comments to EPA's "Tetrachlorvinphos (TCVP) Human Health Draft Risk Assessment for Registration Review", Docket ID: EPA-HQ-OPP-2008-0316*).

5.4.1 Description of Residue Data Used in Dietary Assessment

HED has conducted acute, steady state, and cancer dietary (food and drinking water) exposure and risk assessments using DEEM version 3.16 for TCVP.

The dietary exposure analyses for TCVP are refined. The only food forms included in the analyses are based on animal commodities. The food residues were based upon U. S. Department of Agriculture's Pesticide Data Program (USDA PDP) monitoring data except in a couple of instances where no appropriate PDP data were available (i.e., high-end residues from poultry dermal studies were used for poultry fat and poultry skin). The Biological and Economic Analysis Division (BEAD) of OPP provided percent livestock treated information. Model-derived estimated drinking water concentrations (EDWCs) were provided by the Environmental Fate and Effect Division (EFED). EDWCs were based on spot applications to kennels, poultry droppings, garbage and manure piles, and corrals and were directly incorporated into the assessments as described in Section 5.3 above.

Since the PDP only analyzed for residues of TCVP (and not for TCVP metabolites) a factor was applied to the PDP residues in order to account for all the metabolites of concern for the cancer assessment. The factor was calculated by determining the ratio of parent TCVP to total residues of concern in the livestock residue studies (see Table 2, D436835).

5.4.2 Percent Crop Treated Used in Dietary Assessment

For the acute and steady state analyses, the maximum estimated percent livestock treated of 3% was used for cattle and swine and the estimated maximum of 11% was used for poultry.

For the cancer analysis, the following estimated average percent livestock treated values were used: 1% for dairy cattle, 2% for beef cattle and swine, and 6% for poultry.

5.4.3 Acute Dietary Risk Assessment

The refined acute dietary (food only) exposure analysis resulted in risk estimates above HED's level of concern (exceeded 100% the acute population adjusted dose (aPAD)) at the 99.9th percentile of exposure for the children's population subgroups. The highest exposed subgroup is children 3-5 years old at 190% of the aPAD.

When drinking water is analyzed by itself, the acute dietary (water only) risk estimates are all below HED's level of concern for the U.S. population and all population subgroups at the 95th and 99.9th percentile of exposure.

Most of the exposure from food is due to the high-end residue on chicken skin from poultry dermal studies (residue on uncooked chicken skin from direct dermal spray applications at maximum labeled rates with a 0-day pre-slaughter interval).

Since dietary exposures from food alone were of concern, drinking water exposures were not combined with exposures from food. Combining those exposures would result in even greater risk estimates of concern.

Table 5.4.3.1. Results of Acute Dietary (Food Only) Exposure and Risk Analysis.

Population Subgroup[1]	aPAD[2] (mg/kg/day)	95th Percentile		99th Percentile		99.9th Percentile	
		Exposure (mg/kg/day)	% aPAD	Exposure (mg/kg/day)	% aPAD	Exposure (mg/kg/day)	% aPAD
General U.S. Population	0.0028	0.000022	< 1	0.000680	24	0.002806	100
All Infants (<1 year old)	0.0028	0.000012	< 1	0.000288	10	0.002739	98
Children 1-2 years old	0.0028	0.000069	2.5	0.001073	38	0.004708	170
Children 3-5 years old	0.0028	0.000054	1.9	0.001386	50	0.005230	190
Children 6-12 years old	0.0028	0.000037	1.3	0.000938	33	0.003941	140
Youth 13-19 years old	0.0028	0.000024	< 1	0.000731	26	0.003318	120
Adults 20-49 years old	0.0028	0.000022	< 1	0.000722	26	0.002584	92
Adults 50-99 years old	0.028	0.000011	< 1	0.000492	1.8	0.001690	6.0
Females 13-49 years old	0.0028	0.000020	< 1	0.000651	23	0.002300	82

[1] Population with the greatest exposure is in bold.
[2] aPAD = acute population-adjusted dose.

Table 5.4.3.2. Results of Acute Dietary (Drinking Water Only) Exposure and Risk Analysis.

Population Subgroup[1]	aPAD[2] (mg/kg/day)	95th Percentile		99th Percentile		99.9th Percentile	
		Exposure (mg/kg/day)	% aPAD	Exposure (mg/kg/day)	% aPAD	Exposure (mg/kg/day)	% aPAD
General U.S. Population	0.0028	0.000009	< 1	0.000033	1.2	0.000121	4.3
All Infants (<1 year old)	0.0028	0.000022	< 1	0.000093	3.3	0.000369	13
Children 1-2 years old	0.0028	0.000012	< 1	0.000048	1.7	0.000187	6.7

Table 5.4.3.2. Results of Acute Dietary (Drinking Water Only) Exposure and Risk Analysis.							
Population Subgroup[1]	**aPAD[2] (mg/kg/day)**	**95th Percentile**		**99th Percentile**		**99.9th Percentile**	
		Exposure (mg/kg/day)	**% aPAD**	**Exposure (mg/kg/day)**	**% aPAD**	**Exposure (mg/kg/day)**	**% aPAD**
Children 3-5 years old	0.0028	0.000011	< 1	0.000041	1.4	0.000147	5.2
Children 6-12 years old	0.0028	0.000008	< 1	0.000030	1.1	0.000111	4.0
Youth 13-19 years old	0.0028	0.000006	< 1	0.000025	< 1	0.000095	3.4
Adults 20-49 years old	0.0028	0.000009	< 1	0.000033	1.2	0.000118	4.2
Adults 50-99 years old	0.028	0.000009	< 1	0.000032	< 1	0.000110	< 1
Females 13-49 years old	0.0028	0.000009	< 1	0.000033	1.2	0.000120	4.3

[1] Population with the greatest exposure is in bold.
[2] aPAD = acute population-adjusted dose.

5.4.4 Steady State Dietary Risk Assessment

The refined steady state (food only) exposure analysis resulted in risk estimates above HED's level of concern (exceeded 100% the steady state population adjusted dose (ssPAD)) at the 99.9th percentile of exposure for the children's population subgroups. The highest exposed subgroup is children 3-5 years old at 120% of the ssPAD.

The steady state dietary (water only) risk estimates are all below HED's level of concern for the U.S. population and all population subgroups at the 95th and 99.9th percentile of exposure.

Most of the exposure from food is due to the high-end residue on chicken skin from poultry dermal studies (residue on uncooked chicken skin from direct dermal spray applications at maximum labeled rates with a 0-day pre-slaughter interval).

Since dietary exposures from food alone were of concern, drinking water exposures were not combined with exposures from food. Combining those exposures would result in even greater risk estimates of concern.

Table 5.4.4.1. Results of Steady State Dietary (Food Only) Exposure and Risk Analysis.							
Population Subgroup[1]	**ssPAD[2] (mg/kg/day)**	**95th Percentile**		**99th Percentile**		**99.9th Percentile**	
		Exposure (mg/kg/day)	**% ssPAD**	**Exposure (mg/kg/day)**	**% ssPAD**	**Exposure (mg/kg/day)**	**% ssPAD**
General U.S. Population	0.0028	0.000092	3.3	0.000599	21	0.001994	71
All Infants (<1 year old)	0.0028	0.000020	< 1	0.000299	11	0.001843	66
Children 1-2 years old	0.0028	0.000128	4.6	0.001070	38	0.003181	110
Children 3-5 years old	0.0028	0.000152	5.4	0.001214	**43**	**0.003444**	**120**
Children 6-12 years old	0.0028	0.000130	4.6	0.000782	28	0.002991	110
Youth 13-19 years old	0.0028	0.000116	4.1	0.000645	23	0.002118	76
Adults 20-49 years old	0.0028	0.000112	4.0	0.000621	22	0.001971	70

Table 5.4.4.1. Results of Steady State Dietary (Food Only) Exposure and Risk Analysis.							
Population Subgroup[1]	**ssPAD[2] (mg/kg/day)**	**95th Percentile**		**99th Percentile**		**99.9th Percentile**	
		Exposure (mg/kg/day)	**% ssPAD**	**Exposure (mg/kg/day)**	**% ssPAD**	**Exposure (mg/kg/day)**	**% ssPAD**
Adults 50-99 years old	0.028	0.000049	< 1	0.000418	1.5	0.001105	3.9
Females 13-49 years old	0.0028	0.000098	3.5	0.000572	20	0.001481	53

[1] Population with the greatest exposure is in bold.
[2] ssPAD = steady state population-adjusted dose.

Table 5.4.4.2. Results of Steady State Dietary (Drinking Water Only) Exposure and Risk Analysis.							
Population Subgroup[1]	**ssPAD[2] (mg/kg/day)**	**95th Percentile**		**99th Percentile**		**99.9th Percentile**	
		Exposure (mg/kg/day)	**% ssPAD**	**Exposure (mg/kg/day)**	**% ssPAD**	**Exposure (mg/kg/day)**	**% ssPAD**
General U.S. Population	0.0028	0.000009	< 1	0.000031	1.1	0.000096	3.4
All Infants (<1 year old)	0.0028	0.000024	< 1	0.000088	3.2	0.000300	11
Children 1-2 years old	0.0028	0.000013	< 1	0.000045	1.6	0.000143	5.1
Children 3-5 years old	0.0028	0.000011	< 1	0.000038	1.4	0.000114	4.1
Children 6-12 years old	0.0028	0.000008	< 1	0.000028	< 1	0.000085	3.0
Youth 13-19 years old	0.0028	0.000007	< 1	0.000023	< 1	0.000075	2.7
Adults 20-49 years old	0.0028	0.000009	< 1	0.000031	1.1	0.000094	3.4
Adults 50-99 years old	0.028	0.000009	< 1	0.000030	< 1	0.000087	< 1
Females 13-49 years old	0.0028	0.000009	< 1	0.000031	1.1	0.000095	3.4

[1] Population with the greatest exposure is in bold.
[2] ssPAD = steady state population-adjusted dose.

5.4.5 Cancer Dietary Risk Assessment

The refined cancer dietary (food and drinking water) assessment resulted in an estimated exposure to TCVP and its metabolites containing the 2,4,5 trichlorobenzene moiety (the residues of concern for cancer) of 0.000513 mg/kg/day. Applying the Q_1^* of 0.00183 $(mg/kg/day)^{-1}$ to the exposure value results in a cancer risk estimate of 9×10^{-7}. Drinking water is the major contributor to the cancer dietary risk estimate.

Table 5.4.5.1. Summary of CANCER Dietary Exposure and Risk for Tetrachlorvinphos (and metabolites).						
Population Subgroup	**Food and Water**		**Food Only**		**Water Only**	
	Exposure (mg/kg/day)	**Risk**	**Exposure (mg/kg/day)**	**Risk**	**Exposure (mg/kg/day)**	**Risk**
Adults	0.000513	9×10^{-7}	0.000044	8×10^{-8}	0.000469	8×10^{-7}

6.0 Residential and Non-Occupational Exposure/Risk Characterization

Occupational and Residential Exposure Memo: D436833, 12/21/2016, W. Britton [17]

Residential exposures (handler and post-application) are anticipated from the use of TCVP pet products for dogs and cats including collars, dusts/powders, and pump/trigger sprays. Exposures are expected for adults who apply TCVP products to their pets and from post-application exposures for adults and children who may contact previously treated pets. Residential TCVP handler and post-application exposures are anticipated to be short- (1 to 30 days), intermediate- (1 to 6 months), and long-term (>6 months – *for pet collar scenarios only*). However, because of the steady state AChE inhibition exhibited by the OPs, steady state (typically 21 days and longer for OPs, but 1 day for TCVP) residential exposures were assessed for TCVP pet products.

For adults, when an endpoint is not sex-specific (i.e., the endpoints are based on developmental or fetal effects) a body weight of 80 kg is typically used in risk assessment; however, in this case, a female-specific body weight of 69 kg was used. While the endpoint of concern, RBC AChE inhibition, is not sex-specific, the female body weight was used for pregnant women due to uncertainty in the human dose-response relationship for neurodevelopmental effects.

Following EPA's December 21, 2015 Draft TCVP risk assessment, Bayer HealthCare, Hartz Mountain Corporation, and NRDC submitted comments during the public comment period, primarily regarding the formulation type of pet collars. This document addresses, where appropriate, those comments. A comprehensive response to comments on the TCVP draft human health risk assessment (including ORE-specific comments) is also provided in the following memo: D. Drew et al., Tetrachlorvinphos (TCVP) Health Effects Division Response to Comments on the December 21, 2015 Draft Human Health Risk Assessment for TCVP Registration Review, D433403, 12/21/2016.

Formulation Type Issue: In 2009, the Natural Resources Defense Council (NRDC) petitioned the EPA to cancel all pet uses for the pesticide tetrachlorvinphos (TCVP). In 2014, the agency responded to the 2009 petition by conducting a human health risk assessment for all currently registered TCVP products which include collars, dusts/powders, and pump and trigger spray formulations. That risk assessment was dated Nov. 5, 2014. At that time, no human health risks of concern were identified for any TCVP pet product, and the petition to cancel all pet products was denied on Nov. 6, 2014. The NRDC subsequently responded to the agency's denial with arguments presented in NRDC's Aug. 5, 2015 Opening Brief in *NRDC v. EPA*, Case No. 15-70025 (9th Cir.) (Opening Brief). Among the arguments raised by NRDC was the assertion that the agency incorrectly considered the TCVP flea collar formulation to be a liquid formulated product:

"NRDC states that the EPA failed to 'research' the TCVP flea collar label; instead it ignored the information in the label right on the box regarding the chemical formulation.' [NRDC Opening

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[17] W. Britton *et al.*, 12/21/2016, D436833, Tetrachlorvinphos: Final Occupational and Residential Exposure Assessment for Registration Review

Brief, p.67]. The label for the Hartz UltraGuard Flea and Tick Collar for Dogs (EPA Reg. No. 2596-84) states that 'as the collar begins to work, a fine white powder will appear on the surface.' As a result, NRDC argues that the transfer coefficient (TC) recommended for solid formulations should have been used instead of the transfer coefficent for liquid formulations as is recommended by the 2012 Residential SOPs."[18]

The agency responded to this and all other arguments raised by NRDC in a December 21, 2015 memorandum,[19] issued along with the Draft risk assessment for Registration Review. The following is an excerpt of the agency's response relating to the pet collar formulation issue:

"Per EPA's 2012 Residential SOPs[20]*: Treated Pets, pet collar products are categorized as a liquid formulation. This position was based on research conducted at the time of SOP development that supported that pet collars function by means of diffusion, transferring from the collar to the surrounding area. More specifically, the active ingredient, which is embedded in the collar matrix, diffuses slowly through the matrix, thus controlling the amount of the active ingredient at the collar's surface. The active ingredient available on the surface of the pet collar then "rubs off" or transfers from the collar to the animal's hair coat via embedded lubricants which function as transfer agents at the surface of the collar. Based on the categorization of pet collars as liquid formulations, the assessment of post-application exposures for these product types would be conducted with use of the TCs, and the fraction active ingredient on the hands from TC studies (Fai_{hands}) recommended for the assessment of liquid formulated products as recommended in the 2012 Residential SOPs.*

The information provided by NRDC states that the label for the Hartz UltraGuard Flea and Tick Collar for Dogs (EPA Reg. No. 2596-84) states that "as the collar begins to work, a fine white powder will appear on the surface." HED has confirmed that this statement is present on the current labeling for the identified product and that an identical statement is also found on the following TCVP pet collar products (5 of 9 total pet collar products): EPA Reg. Nos. 2596-62, 2596-63, 2596-83, 2596-84, and 2596-139. Taking label statements into account, and based upon further research which suggests that some pet collars may act by extrusion of the active ingredient from the collar matrix as a fine dust, HED has reconsidered the position that the TCVP pet collars are all liquid formulated products. As a result of this uncertainty, in the TCVP draft human health risk assessment in support of registration review, HED has updated the assessment of post-application risks from TCVP pet collars in consideration of both the dust- and liquid-specific TCs and Fai_{hands} recommended SOP values."[21]

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[18] W. Britton. Tetrachlorvinphos (TCVP): Responses to Arguments Presented in the Natural Resources Defense Council, Inc.'s (NRDC) Aug. 5, 2015 Opening Brief in *NRDC v. EPA*, Case No. 15-70025 (9th Cir.). 12/21/15, D430589, at 8 (summarizing NRDC's argument).

[19] *Id.*

[20] http://www2.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide

[21] *Id.* at 8-9.

In response to the 2015 Draft TCVP risk assessment, Bayer HealthCare submitted comments to address the formulation type issue. Bayer agreed with the approach employed by the agency, stating: "*Based on the NRDC assertion and the statement on the collar packaging the agency has taken the understandable approach of calculating the post-application exposure, using both liquid and solid formulation transfer coefficients, until the uncertainty is resolved.*" Bayer proceeded to address the formulation type issue by describing how the active ingredient is released from the collar and distributed on the animal. Bayer described that, "*To achieve their goal of effective pest control, the flea collars are designed to deliver the insecticide from the collar in either a liquid or solid state. The collar is made from a mixture of plastic resins and resin modifiers. The resins are formulated to have appropriate strength and flexibility so the collar can withstand the shaping operations without cracking or crumbling. The resins must also have appropriate release characteristics, such that the TCVP (or other insecticide active ingredient) can escape the collar at the proper rate, while inert components remain in the collar.*"

Per Bayer, TCVP is distributed on the animal by abrasion or movement against the animal or diffusion from the animal's body heat. "*Within a few days after manufacture, the insecticide begins to migrate from within the body of the collar and form a coating of particles, resembling a dust or powder on the surface of the collar. As the particles of the active ingredient are displaced or shaken from the surface due to the normal activity of the animal, additional particles appear by migration from the body of the composition to replace the insecticide particles displaced from the surface (i.e., the displaced particles are replenished continuously). This describes the typical release mechanism and explains the presence of the powder as raised by NRDC. The powders are in the immediate vicinity of the collar; however, this is not necessarily the form in which the insecticide is dispersed to the animal or relevant to the transfer coefficient.*" They continued to describe that the sebaceous glands within the dog's skin that lubricate the hair are the mechanism for dispersion of the insecticide. "*Insecticides that are used in flea collars are lipophilic and soluble in the animal's skin oils. So, even though the collars may release some of the insecticides as a solid they are dispersed along the animal's body as a solution or suspension in the animal's skin via the natural skin oils.*" As such, the assessment of human health risks from TCVP pet collars were conducted in a manner that accounts for the likelihood of the presence of both liquid and solid forms while considering the isolated location (i.e., the head/neck) of ai in the dust/powder form.

While informative, Bayer's comments pose a dilemma for the agency. Although they describe the mechanism of dispersion of active ingredient along the animal's body as a solution or suspension in the skin, they also indicate that the insecticide begins to migrate from within the collar as a "coating of particles, resembling a dust or powder form on the surface of the collar" and that "flea collars are designed to deliver the insecticide from the collar in either a liquid or solid state." The mechanism of active ingredient dispersion via the skin alone is not adequate to describe the potential for post-application exposures. If the active ingredient is present as a liquid or particulate or dust on the surface of the pet collar, it could be transferred in either form from the collar to the pet's fur immediately surrounding and result in the potential for post-application exposures from either direct contact with the pet collar, or the surrounding fur.

Formulation Type Approach: A unique approach has been applied in order to account for the potential for exposures from the presence of TCVP to exist as both liquid and solid forms concurrently. The approach uses the same methodologies described in the 2012 Residential SOPs for assessment of residential handler and post-application exposure assessment for pet collar usage. However, whereas the 2012 Residential SOPs recommend that pet collars be assessed as a liquid formulation, the present approach assesses pet collar exposures as both a liquid and solid form. For residential handlers, this means use of the liquid UE data as recommended by the 2012 Residential SOPs and chemical-specific dust UE data for these formulation types. For the residential post-application exposure assessment, this means use of transfer coefficients (dermal exposures) and the fraction of active ingredient on hands from the transfer coefficent studies (hand-to-mouth exposures) specific to both liquid and solid formulation types.

The individual dust and liquid formulation handler and post-application doses were estimated, and then another step was included in the assessment where the liquid and dust doses were averaged assuming a ratio of liquid to dust in the collar formulation. For both handler and post-application scenarios, ratios of 1/99, 50/50, and 99/1 liquid/dust were assumed to cover a range of potential exposures.

The methodologies and inputs used for the individual formulation assessments for residential handlers and residential post-application exposures are described in Appendix B of the corresponding ORE memo (Memo, W. Britton *et al*, D436833).

Due to NRDC's argument related to the TCVP pet collar formulation, the agency has begun efforts to reevaluate pet collar formulation type to carefully consider whether pet collar products are more closely related to more traditional liquid formulation pet products such as shampoos and spot-ons, or solid formulated products such as dusts and powders. In following with this evaluation, the agency intends to request and review additional information relating to all registered pet collar products as they undergo registration review, as well as any proposed new pet collar uses. This evaluation will continue until the agency is satisfied that, based on the design and operation of pet collar products, a final formulation type decision can be made along with recommendations for human health risk assessment of exposures to pet collar-treated pets.

6.1 Residential Handler Exposures

HED uses the term "handlers" to describe those individuals who are involved in the pesticide application process. HED believes that there are distinct tasks related to applications and that exposures can vary depending on the specifics of each task. Residential handlers are assumed to complete all elements of an application without use of any protective equipment.

Residential handler exposures to TCVP pet products may occur via the dermal or inhalation routes while the product is placed on a cat or dog. Both steady state non-cancer and cancer residential handler exposure assessments were performed for adult homeowners applying TCVP pet collars, dusts/powders, and pump/trigger sprays products to cats and dogs. Since there is no non-cancer dermal hazard for TCVP, the steady state (non-cancer) handler assessment includes only inhalation exposures. For the cancer assessment, both dermal and inhalation exposures are

assessed.

The exposure data and assumptions that underlie the residential handler non-cancer risk estimates can be referenced in the 2014 residential assessment[22] and the 2012 Residential SOPs. The algorithms used to estimate non-cancer exposure and dose for residential handlers can be found in Appendix B of the corresponding ORE assessment (Memo, W. Britton *et al.*, D436833) and/or the 2012 Residential SOPs.[23]

Due to the uncertainty associated with whether TCVP pet collars are liquid and/or dust formulated products, residential handler steady state inhalation exposures for TCVP pet collar application were assessed (as described above in Section 6.0) assuming pet collars could be liquid and solid (dust) formulations concurrently, with varying ratios liquid/dust. When assuming the TCVP pet collars are a liquid formulation, the liquid-specific unit exposures (UE) values (i.e., surrogate data from a spot-on applicator study) from the 2012 Residential SOPs were used. When assuming the pet collars are a solid formulation, HED used the best available data, a TCVP dust/powder applicator exposure study (MRID 45519601).

The liquid formulation spot-on surrogate UE data assumes negligible inhalation exposure; therefore, only the dust-specific UE data (i.e., a TCVP dust/powder applicator exposure study) is expected to result in the potential for inhalation exposures. In the case of handlers, therefore, the dust formulation drives any potential exposure.

Summary of Residential Handler Non-Cancer Exposure and Risk Estimates

Pet Collars: Because there is uncertainty whether the TCVP pet collars are liquid and/or dust formulated products, residential handler (adults) steady state inhalation exposures were evaluated assuming both liquid and solid (dust) formulations are present concurrently with varying ratios of liquid/dust. No inhalation risks of concern were identified for residential handlers for any liquid/dust formulation ratio assumption. When assuming a ratio of 1/99 liquid/dust, MOEs range from 920 to 4,600; when assuming a ratio of 50/50 liquid/dust, MOEs range from 1,800 to 9,100; and when assuming a ratio of 99/1 liquid/dust, MOEs range from 91,000 to 450,000 (LOC = 300).

Dust/Powder and Pump/Trigger Spray: All residential handler (adults) non-cancer steady state inhalation risks estimated for the TCVP pet dust/powder pump/trigger spray formulations are not of concern (i.e., all MOEs are > 300; LOC = 300; range = 3,200 to 160,000).

A summary of residential handler exposures and risks is presented in Appendix G.

Residential Handler Cancer Exposure and Risk Estimate Equations

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[22] W. Britton. Residential Exposure Assessment in Response to the Natural Resources Defense Council Petition to Cancel All Pet Uses for Tetrachlorvinphos. 11/05/2014. D420283.

[23] http://www2.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide

Cancer risk estimates were calculated using a linear low-dose extrapolation approach in which a Lifetime Average Daily Dose (LADD) is first calculated and then compared with a Q_1^* that has been calculated for TCVP based on dose response data in the appropriate toxicology study (Q_1^* = 1.83 x 10^{-3} $(mg/kg/day)^{-1}$). Absorbed average daily dose (ADD) levels were used as the basis for calculating the LADD values. Dermal and inhalation ADD values were first added together to obtain combined ADD values. LADD values were then calculated and compared to the Q_1^* to obtain cancer risk estimates.

The exposure data and assumptions that underlie the residential handler cancer risk estimates can be found in the 2014 residential assessment[24] and the 2012 Residential SOPs. The algorithms used to estimate the LADD and cancer risk for residential handlers can be found in Appendix B of the corresponding ORE assessment (Memo, W. Britton *et al.*, D436833).

Summary of Residential Handler Cancer Exposure and Risk Estimates

Pet Collars: Residential handler cancer risks (combined dermal and inhalation) estimated for TCVP pet collars assuming a 1/99 liquid/dust formulation ratio are all 10^{-7}. When assuming a 50/50 liquid/dust formulation ratio (use of liquid-specific and dust-specific UE data) are all 10^{-7}. When assuming a 99/1 liquid/dust formulation for pet collars, the residential handler cancer risk estimates are all 10^{-8}.

Dust/Powder and Pump/Trigger Spray: Residential handler estimated cancer risks (combined dermal and inhalation) for TCVP dusts/powders range from 10^{-9} to 10^{-7}, and for pump/trigger sprays range from 10^{-9} to 10^{-8}.

A summary of residential handler cancer exposures and risks is presented in Appendix H.

6.2 Residential Post-application Exposure/Risk Estimates

There is the potential for post-application exposure for individuals exposed as a result of contacting a cat/dog previously treated with TCVP pet products (dusts/powders, pump/trigger sprays, pet collars). The quantitative exposure/risk assessment for residential post-application exposures is based on the following scenario:

1) Post-application incidental oral (hand-to-mouth) exposure (children 1 to < 2 years olds only) from contacting cats and dogs treated with TCVP.

Since there is no non-cancer dermal hazard for TCVP, a quantitative non-cancer post-application dermal exposure assessment was not performed for adults or children. A quantitative residential post-application inhalation exposure assessment was not performed as inhalation exposure is expected to be negligible from applications to pets.

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[24] W. Britton. Residential Exposure Assessment in Response to the Natural Resources Defense Council Petition to Cancel All Pet Uses for Tetrachlorvinphos. 11/05/2014. D420283.

The lifestages selected for each post-application scenario (i.e., children 1 to < 2 years old) are based on an analysis provided as an Appendix in the corresponding ORE assessment (Memo, W. Britton *et al.*, D436833) and the 2012 Residential SOPs.[25] While not the only lifestage potentially exposed for these post-application scenarios, the lifestage that is included in the quantitative assessment is health protective for the exposures and risk estimates for any other potentially exposed lifestage.

Residential Non-Cancer Post-Application Exposure Data and Assumptions

A series of assumptions and exposure factors served as the basis for completing the residential non-cancer post-application risk assessment. The exposure data and assumptions that underlie the residential non-cancer post-application risk estimates can be found in the 2014 residential assessment[26] and the 2012 Residential SOPs.

Several inputs and assumptions that underlie the residential post-application risk assessment of TCVP pet products were addressed previously by EPA in the responses to NRDC's August 5, 2015 Opening Brief,[27] including: the use of the Davis study; TCVP pet collar product formulation type; daily exposure time spent in contact with TCVP treated pets; indirect hand-to-mouth activity; and the application of transferable residue data in EPA's risk assessment algorithms. NRDC has repeated all of these same arguments in its comments submitted for the 2015 DRA. EPA has addressed the use of the Davis study and TCVP pet collar product formulation type arguments herein. The agency's responses to all other arguments remain the same as addressed previously.

Residue Transfer Assumptions: Chemical-specific residue transfer studies were used for assessment of post-application exposures from registered TCVP pet products.

Dust/Powder and Pump/Trigger Spray: Consistent with the 2015 draft ORE assessment for Registration Review, a TCVP powder and pump spray study (MRID 45485501) was used to assess post-application exposure for these scenarios. A summary and discussion of the use of these data was included in the 2014 residential risk assessment. As described in the 2014 residential risk assessment, the TCVP powder and pump spray post-application exposure study was not conducted in a manner reflective of current standards that require a defined stroking procedure and greater number of petting simulations. In order to account for this difference, the agency used the maximum observed percent residue transfer on the day of product application (Day 0) for both formulations for exposure and risk quantification. Typically, the agency assesses post-application risk with use of the mean percent residue transfer measured on Day 0;

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[25] Available: http://www2.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide

[26] W. Britton. Residential Exposure Assessment in Response to the Natural Resources Defense Council Petition to Cancel All Pet Uses for Tetrachlorvinphos. 11/05/2014. D420283.

[27] W. Britton, Tetrachlorvinphos (TCVP): Responses to Arguments Presented in the Natural Resources Defense Council, Inc.'s (NRDC) Aug. 5, 2015 Opening Brief in *NRDC v. EPA*, Case No. 15-70025 (9th Cir.). 12/21/15, D430589.

the use of the maximum value results in a more health protective risk assessment. Even though the post-application exposure study methods have evolved, the TCVP study employed a rigorous collection method and is not anticipated to underestimate exposure.

The 2012 Residential SOPs: Treated Pets recommends assessment of post-application exposures using day of application (i.e., Day 0) residue transfer -- defined as fraction application rate (F_{AR}) in the 2012 SOPs. Day of application (Day 0) percent residue transfer values used in the 2014 residential risk assessment for exposure/risk quantification of dusts/powders and pump/triggers sprays are as follows: dusts/powders, 0.048% (maximum observed) and pump sprays, 0.81% (maximum observed).

Pet Collar Exposure Data Source: The 2015 draft ORE assessment for Registration Review used both the Davis study and an amitraz pet collar residue transfer study for assessment of non-cancer residential post-application risks following contact with pets treated with TCVP pet collars. The Davis study publication was considered for use in the assessment due to arguments submitted by NRDC in its August 5th, 2015, Opening Brief in *NRDC v. EPA*, Case No. 15-70025 (9th Cir.) (Opening Brief). NRDC's Opening Brief was filed in litigation challenging EPA's Nov. 6, 2014 denial of NRDC's 2009 petition to cancel all TCVP pet products; the denial was based on the 2014 residential pet product assessment. The agency provided a point-by-point response to the NRDC's arguments in a Dec. 21, 2015 memorandum,[28] issued in conjunction with the Dec. 21, 2015 Draft TCVP Risk Assessment for Registration Review. Among the arguments presented by NRDC was that the agency "failed to consider the Davis study for the estimation of post-application risks for exposures to the TCVP pet collar." In its 2015 memorandum, the agency acknowledged consideration of the potential effect of using the Davis study as the basis for residential post-application assessment of exposures from TCVP pet collars, the study was reviewed,[29] an OPP ethics review was conducted[30], and preliminary risk estimates were presented with use of these data. However, the formal use of the Davis study was put on hold pending review by EPA's HSRB in January 2016. The Davis study includes 1) glove residue data collected by adult volunteers petting TCVP treated dogs 2) plasma cholinesterase (ChE) measures from treated dogs 3) tee shirt samples collected from children exposed to TCVP treated dogs and 4) urinary biomonitoring for adults and children exposure to TCVP treated dogs. However, for purposes of the TCVP risk assessment, EPA may rely only on the transferable residue data [in light of 40 CFR Part 26, subpart Q regarding ethical standards for assessing whether to rely on the results in human research in EPA actions] as these are the only data from the study that result in the potential for greater risks, are applicable to human exposures (in the case of the dog plasma ChE measures), or in the case of the urinary biomonitoring data, are useful given current scientific limitations (i.e., a physiologically based pharmacokinetic (PBPK) model applicable to TCVP). While EPA proposed to rely only on the

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[28] W. Britton. Tetrachlorvinphos (TCVP): Responses to Arguments Presented in the Natural Resources Defense Council, Inc.'s (NRDC) Aug. 5, 2015 Opening Brief in *NRDC v. EPA*, Case No. 15-70025 (9th Cir.). 12/21/15, D430589.

[29] W. Britton. Science Review of "Davis et al., 2008. Assessing Intermittent Pesticide Exposure from Flea Control Collars Containing the Organophosphorus Insecticide Tetrachlorvinphos" for HSRB Consideration. D430707. 12/16/2015.

glove residue data (which did not involve children), since these data were collected as part of broader research which did involve children, HSRB review was necessary.

On January 12-13, 2016, the EPA HSRB addressed the scientific and ethical charge questions related to Davis study. Ethics and science reviews were conducted by the agency in support of the HSRB meeting.[30,31] A Federal Register (FR) notice was published on 4/11/2016 (69 FR 21335) and provides the following information: EPA's proposal to rely on the Davis study; the reason for review by HSRB; the background on ethical conduct of research; summary of discussion on ethics-related questions; the standards applicable to ethical conduct and reliance on data; and the availability of HSRB meeting materials.[32]

The HSRB concluded that, "The research is scientifically sound and, if used appropriately, the pet fur transferable residue data from the rubbing protocol used in the study can provide useful information for evaluating potential exposures of adults and children from contact with dogs treated with tetrachlorvinphos containing pet collars."[33] Per EPA's response to NRDC's Opening Brief arguments, "EPA would rely on these data (Davis study) for regulatory decision making if HSRB determines that the study is scientifically valid and it meets appropriate human ethics requirements," since these data result in greater potential risks than those estimated using the amitraz pet collar residue transfer study (which had been relied upon in the previous risk assessments). Accordingly, post-application risks have been assessed with use of the Davis study data only and are presented herein.

The use of the Davis study as the primary data source is consistent with, and supported by, the recommendations from the comments following the 2015 draft ORE assessment for Registration Review including those submitted by NRDC and the Hartz Mountain Corporation. Per NRDC, "the Davis Study has met the appropriate scientific and ethical criteria and should be relied upon for the evaluation of exposures from TCVP containing flea collars," and the Hartz Mountain Corporation describes that, "the glove residue data measured in the Davis et al. (2008) study are valuable because they represent actual measurements of TCVP transfer from dogs wearing commercial collars to the hands of individuals petting them." Further, NRDC states that, "EPA's utilization of transferable residue data from the amitraz study is not supported by the evidence and should not be relied upon to evaluate risk."

A summary of the Davis study and a description of how these data have been used for risk quantitation is detailed in Section 5.2 of the corresponding ORE memo (D436833).

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[30] M. Lydon. Ethics Review of Davis et al Research on Flea Collars with TCVP. 12/15/2015.

[31] W. Britton. Science Review of "Davis et al., 2008. Assessing Intermittent Pesticide Exposure from Flea Control Collars Containing the Organophosphorus Insecticide Tetrachlorvinphos" for HSRB Consideration. D430707. 12/16/2015.

[32] https://www.federalregister.gov/documents/2016/04/11/2016-08281/tetrachlorvinphos-tcvp-epa-proposal-to-rely-on-data-from-human-research-on-tcvp-exposure-from-flea

[33] Letter from Liza Dawson, PhD, Chair of the EPA HSRB to Thomas Burke, PhD, MPH, EPA Science Advisor. Subject: January 12-13, 2016 EPA Human Studies Review Board Meeting Report. March 30, 2016.

Residential Non-Cancer Post-application Exposure and Risk Equations

The algorithms used to estimate non-cancer exposure and dose for residential post-application can be found in Appendix B of D436833 and the 2012 Residential SOPs.

Summary of Residential Post-Application Non-Cancer Exposure and Risk Estimates

Pet Collars: As noted above, the post-application assessments for the TCVP pet collars were performed assuming pet collars could be either liquid or solid (dust) formulations, and assuming a varying liquid/dust exposure potential. All child 1 to <2 years old incidental oral exposures to pets treated with pet collars, regardless of the ratio of liquid/dust assumed, are estimated to be of concern (i.e., MOEs < 1000). When assuming a 1/99 liquid/dust formulation ratio, MOEs range from 0.91 to 7.4. When assuming a 50/50 liquid/dust formulation, MOEs range from 1.8 to 15, and when assuming a 99/1 liquid/dust formulation, MOEs range from 65 to 530. A summary of residential post-application exposures and risks from TCVP pet products is presented in Appendix I.

Dust/Powder and Pump/Trigger Spray: Residential post-application steady state non-cancer child 1 to < 2 years old incidental oral (hand-to-mouth) exposures to pets treated with TCVP dust/powders are estimated to be of concern (i.e., MOEs < 1000; MOE range from 98 to 640). However, child 1 to < 2 years old incidental oral exposures to pets treated with TCVP pump/trigger spray products are estimated not to be of concern (i.e., MOEs are > 1,000; MOE range from 1,600 to 15,000).

Residential Cancer Post-Application Exposure Data and Assumptions

A series of assumptions and exposure factors served as the basis for completing the residential cancer post-application risk assessment. All exposure data and assumptions that underlie the residential post-application cancer risk estimates can be referenced in the 2014 residential assessment. Note: For purpose of quantification of estimated TCVP post-application cancer risks, HED used average percent residue transfer data for all days sampled from chemical-specific exposure data for all pet formulations assessed (i.e., the TCVP powder and pump spray study and the Davis study).

Residential Cancer Post-application Exposure and Risk Estimate Equations

As was done for residential handlers, cancer post-application risk estimates for adults were calculated using a linear low-dose extrapolation approach in which a LADD is first calculated and then compared with a Q_1^* that has been calculated for TCVP based on dose response data in the appropriate toxicology study ($Q_1^* = 1.83 \times 10^{-3}$ $(mg/kg/day)^{-1}$). The algorithms used to estimate the LADD and cancer risk for residential post-application exposure can be found in Appendix B of D436833.

It should be noted that in the past, cancer risk assessments have assumed that children are no more sensitive than adults to carcinogens (i.e., no adjustment was made to children's exposure estimates in calculating a cumulative lifetime exposure). More recently, the agency's

"Guidelines for Carcinogen Risk Assessment" (USEPA, 2005) and "Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens" (USEPA, 2005) proposed age-dependent adjustment factors to be applied to children's exposure. These age-dependent factors are applied only to carcinogens shown to have a mutagenic mode of action. In general, most carcinogenic pesticides have not been shown to act through a mutagenic mode of action, and thus separate assessment of children and adults is not warranted. Any pesticide found to be a carcinogen acting through a mutagenic mode of action should be dealt with on a case by case basis, and such an assessment should follow the agency's 2005 guidance. Once the results of the newly-required mutagenicity studies have been submitted and reviewed, the need for an updated cancer assessment will be determined.

Summary of Residential Post-application Cancer Exposure and Risk Estimates

Pet Collars: Residential cancer (adult only) risk estimates for TCVP pet collars assuming a 1/99 liquid/dust formulation ratio range from 10^{-5} to 10^{-4}. When assuming a 50/50 liquid/dust formulation ratio, cancer risk estimates range from 10^{-5} to 10^{-4}. When assuming a 99/1 liquid/dust formulation ratio, cancer risk estimates range from 10^{-6} to 10^{-5}.

Dust/Powder and Pump/Trigger Spray: Residential cancer (adult only) risks estimated for TCVP dust/powder products range from 10^{-7} to 10^{-6}, and for TCVP pump/trigger sprays are all 10^{-7}.

Adult residential post-application dermal cancer risk estimates are presented in Appendix J.

6.3 Spray Drift

A quantitative spray drift assessment was not conducted because the use of TCVP for direct animal treatment to livestock and their premises, in kennels, outdoors as a perimeter treatment, and as a flea treatment on cats and dogs are either 1) not applied via aircraft, groundboom, or airblast equipment or 2) for applications to poultry buildings with groundboom equipment, the use is indoors and not anticipated to be a significant source of spray drift.

6.4 Residential Bystander Post-Application Inhalation Exposure

A quantitative residential post-application inhalation exposure assessment was not performed, as inhalation exposure is expected to be negligible from applications to pets.

7.0 Aggregate Exposure/Risk Characterization

In accordance with the FQPA, for food use pesticides, aggregate risk assessment must consider exposures from three sources: food, drinking water, and residential uses. These exposures could occur from three major routes: oral, dermal, and inhalation. In an aggregate assessment, exposures from relevant sources are added together and compared to quantitative estimates of hazard (e.g., a NOAEL or PAD), or the risks themselves can be aggregated. When aggregating

exposures and risks from various sources, HED considers both the route and duration of exposure.

7.1 Acute Aggregate Risk

The acute aggregate risk assessment combines exposures to TCVP from food and drinking water. While drinking water exposures alone were not of concern, there are acute risk estimates of concern for food only; therefore, a quantitative acute aggregate risk assessment was not conducted.

7.2 Steady State Aggregate Risk

The steady state aggregate assessment includes the steady state dietary (food and water) and residential exposures. However, because there are risks of concern associated with both dietary (food) and residential exposure, a quantitative steady state aggregate risk assessment was not conducted.

7.3 Cancer Aggregate Risk

The cancer aggregate risk assessment combines residential and dietary (food and drinking water) expected lifetime exposures for adults. For TCVP, a cancer aggregate assessment was performed for adult handlers and for adult post-application activities related to residential pet product use.

The residential handler cancer aggregate assessment uses exposures from applying TCVP products to pets (collars, dust/powders, and pump/trigger sprays). Residential handler cancer (dermal) risk estimates for TCVP pet collars assuming a 1/99 liquid/dust formulation ratio are all 10^{-7}. When assuming a 50/50 liquid/dust formulation ratio, cancer risk estimates are all 10^{-7}. When assuming a 99/1 liquid/dust formulation for pet collars, the residential handler cancer risk estimates are all 10^{-8}. Residential handler estimated cancer risks (combined dermal and inhalation) for TCVP dusts/powders range from 10^{-9} to 10^{-7}, and for pump/trigger sprays range from 10^{-9} to 10^{-8}. The cancer dietary (food and drinking water) assessment resulted in an estimated risk of 9×10^{-7}. The cancer aggregate assessment combines the highest (worst case) handler exposure for each pet product formulation type with dietary exposure; this results in aggregate cancer risk estimates that are protective of exposures to other registered pet products of the same formulation type.

The cancer aggregate (dietary and residential exposures) risk estimates for handlers are in the 10^{-7} to 10^{-6} range and are presented in Table 7.3.1.

The residential post-application cancer aggregate assessment uses dermal exposures from contacting pets treated with TCVP products (collars, dust/powders, and pump/trigger sprays). Residential cancer post-application risk estimates for TCVP pet collars assuming a 1/99 liquid/dust formulation ratio range from 10^{-5} to 10^{-4}. When assuming a 50/50 liquid/dust formulation ratio, cancer risk estimates range from 10^{-5} to 10^{-4}. When assuming a 99/1

liquid/dust formulation ratio, cancer risk estimates range from 10^{-6} to 10^{-5}. Post-application cancer risks estimated for handlers of the TCVP dust/powder products range from 10^{-7} to 10^{-6}, and for TCVP pump/trigger sprays are all 10^{-7}. The cancer aggregate assessment combines the highest (worst case) post-application exposure for each pet product formulation type with dietary exposure; this results in aggregate cancer risk estimates that are protective of exposures to other registered pet products of the same formulation type.

The cancer aggregate (dietary and residential exposures) post-application risk estimates are in the 10^{-6} to 10^{-4} range and are presented in Table 7.3.2.

Table 7.3.1. Adult Handler Aggregate Cancer Risk Estimates for TCVP Pet Products
(Risk is estimated using a Q* of 0.00183)

Product Formulation Type	Reg No.; Animal type; Animal size	Food and Water Exposure (mg/kg/day)[1]	Residential Exposure (LADD, mg/kg/day)[2]	Aggregate Cancer Risk (food, water, residential)
Pet Collar (1/99 liquid/dust assumption)	2596-139: Cat; Any	5.1×10^{-4}	1.1×10^{-4}	1×10^{-6}
Pet Collar (50/50 liquid/dust assumption)	2596-139: Cat; Any	5.1×10^{-4}	5.9×10^{-5}	1×10^{-6}
Pet Collar (99/1 liquid/dust assumption)	2596-139: Cat; Any	5.1×10^{-4}	8.5×10^{-6}	9×10^{-7}
Dust/Powder	67517-82: Dog; Large	5.1×10^{-4}	2.3×10^{-4}	1×10^{-6}
Pump/Trigger Spray	2596-125, -140: Dog (Trigger); Large	5.1×10^{-4}	3.9×10^{-5}	1×10^{-6}

[1] Table 5.4.5.1
[2] Appendix D of ORE Memo D436833.
[3]Aggregate Cancer Risk = (Q_1*) (Food & Water Exposure + Residential LADD)

Table 7.3.2. Adult Post-Application Aggregate Cancer Risk Estimates for TCVP Pet Products
(Risk is estimated using a Q* of 0.00183)

Product Formulation Type	Reg No.; Animal type; Animal size	Food and Water Exposure (mg/kg/day)[1]	Residential Exposure (LADD, mg/kg/day)[2]	Aggregate Cancer Risk (food, water, residential)
Pet Collar (1/99 liquid/dust assumption)	2596-139: Dog; Small	5.1×10^{-4}	3.4×10^{-1}	6×10^{-4}

Table 7.3.2. Adult Post-Application Aggregate Cancer Risk Estimates for TCVP Pet Products *(Risk is estimated using a Q* of 0.00183)*				
Product Formulation Type	**Reg No.; Animal type; Animal size**	**Food and Water Exposure (mg/kg/day)[1]**	**Residential Exposure (LADD, mg/kg/day)[2]**	**Aggregate Cancer Risk (food, water, residential)**
Pet Collar (50/50 liquid/dust assumption)	2596-139: Dog; Small	5.1×10^{-4}	1.8×10^{-1}	3×10^{-4}
Pet Collar (99/1 liquid/dust assumption)	2596-139: Dog; Small	5.1×10^{-4}	1.6×10^{-2}	3×10^{-5}
Dust/Powder	2596-78: Cat; Small	5.1×10^{-4}	1.9×10^{-3}	2×10^{-6}
Pump/Trigger Spray	2596-126, 140: Cat (Trigger); Small	5.1×10^{-4}	5.3×10^{-4}	2×10^{-6}

[1] Table 5.4.5.1
[2] Appendix F of ORE Memo D436833.
[3]Aggregate Cancer Risk = (Q_1*) (Food & Water Exposure + Residential LADD)

8.0 Occupational Exposure/Risk Characterization

Occupational and Residential Exposure Memo: D436833, 12/21/2016, W. Britton.

Occupational handler risks have been updated herein to reflect changes in the policy used for inhalation assessment since the 2015 ORE assessment. Previously, HED was using multiple human equivalent doses (HEDs) specific to different handler activities. The current policy recommends that only a single HED is necessary to assess all potential occupational handler activities. All other occupational handler data, assumptions, and algorithms used for the 2015 ORE assessment remain the same.

For adults, when an endpoint is not sex-specific (i.e., the endpoints are based on developmental or fetal effects) a body weight of 80 kg is typically used in risk assessment; however, in this case, a female-specific body weight of 69 kg was used. While the endpoint of concern, RBC AChE inhibition, is not sex-specific, the female body weight was used for pregnant women due to uncertainty in the human dose-response relationship for neurodevelopmental effects.

8.1 Occupational Handler Exposure/Risk Estimates

HED uses the term handlers to describe those individuals who are involved in the pesticide application process. HED believes that there are distinct job functions or tasks related to applications and exposures can vary depending on the specifics of each task. Job requirements (amount of chemical used in each application), the kinds of equipment used, the target being treated, and the level of protection used by a handler can cause exposure levels to differ in a manner specific to each application event.

Based on the anticipated use patterns and current labeling, types of equipment and techniques that can potentially be used, occupational handler exposure is expected from the proposed uses.

The quantitative exposure/risk assessment developed for occupational handlers is based on the following scenarios:

Mixer/Loaders:

(1a) Liquid: Groundboom Applications
(1b) Liquid: Paint Applications
(2a) Wettable Powder: Groundboom Applications
(2b) Wettable Powder: Paint Applications
(3a) Dust: Paint Applications

Applicators:

(4) Groundboom Applications
(5) Open Pour Liquid Additive for Feed Through
(6a) RTU Pet Collar – 1/99 Liquid/Dust Formulation
(6b) RTU Pet Collar – 50/50 Liquid/Dust Formulation
(6c) RTU Pet Collar – 99/1 Liquid/Dust Ratio Formulation
(7) RTU Dust/Powder – Pets
(8) RTU Pump/Trigger Sprays - Pets

Mixer/Loader/Applicators:

(9a) Liquid: Backpack Sprayer
(9b) Liquid: Manually-Pressurized Handwand
(9c) Liquid: Mechanically-Pressurized Handgun
(9d) Liquid: Backrubber or Facerubber
(10a) Wettable Powder: Backpack Sprayer
(10b) Wettable Powder: Manually-Pressurized Handwand
(10c) Wettable Powder: Mechanically-Pressurized Handgun
(10d) Wettable Powder: Fogging Equipment (handheld, portable, and stationary)
(10e) Wettable Powder: Rotary Duster
(10f) Wettable Powder: Plunger Duster
(11a) Dust: Self-Treating Dust Bag
(11b) Dust: Shaker Can
(11c) Dust: Rotary Duster
(11d) Dust: Plunger Duster
(12a) Paint: Brush or Roller
(12b) Paint: Airless Sprayer
(13) Solid Feed Additive for Feed Through: Cup

Occupational Handler Exposure Data and Assumptions
A series of assumptions and exposure factors served as the basis for completing the occupational handler risk assessments. Each assumption and factor is detailed below on an individual basis. Application rate: A summary of all TCVP occupational use sites and application rates is presented in Appendix A of D436833.

Pet Collar Formulation Assumptions: As was mentioned in the residential sections, due to the uncertainty associated with whether TCVP pet collars are liquid and/or dust formulated products, handler steady state inhalation exposures for TCVP pet collar application were assessed assuming pet collars could be liquid and solid (dust) formulations concurrently with varying ratios of liquid/dust. The liquid formulation UE data assumes negligible inhalation exposure; therefore, only the dust-specific UE data is expected to result in the potential for inhalation exposures. In the case of handlers, therefore, the dust formulation drives any potential exposure.

Unit Exposures: It is the policy of HED to use the best available data to assess handler exposure. Sources of generic handler data, used as surrogate data in the absence of chemical-specific data, include PHED 1.1, the AHETF database, the Outdoor Residential Exposure Task Force (ORETF) database, or other registrant-submitted occupational exposure studies. Some of these data are proprietary (e.g., AHETF data), and subject to the data protection provisions of FIFRA. The standard values recommended for use in predicting handler exposure that are used in this assessment, known as "unit exposures", are outlined in the "Occupational Pesticide Handler Unit Exposure Surrogate Reference Table[34]", which, along with additional information on HED policy on use of surrogate data, including descriptions of the various sources, can be found at the agency website[35].

A single chemical-specific exposure study, Monitoring Exposure of Mixer/Loaders and Applicators Treating Agricultural Premises with Tetrachlorvinphos (Rabon® 50 WP Insecticide) in Handheld Wand-Type Sprayers (MRID 42622301), was used as appropriate (i.e., exposure scenario 10c, mix/load and apply WP with mechanically-pressurized handgun) in the most recent occupational risk assessment for TCVP.[36] Per the prior risk assessment, risks for the exposure scenario were estimated with use of the chemical-specific exposure data as well as surrogate PHED data. This exposure study was summarized in the 2015 draft ORE assessment Registration Review[37].

The PHED data recommended for the exposure scenario reflects unit exposure values (dermal and inhalation) that represent an individual conducting all activities, mixing/loading/applying, for use of the WP product by mechanically pressurized handgun. In contrast, the chemical-specific exposure study was conducted in a manner which separated out the mixing/loading and application components of the exposure scenario. Exposure scenario 10c has been assessed, and estimated risks presented separately, (i.e., mixer/loader and applicator) with use of the chemical-specific data, and for all activities with use of PHED. When applied, the dermal and inhalation unit exposures resulting for product application result in risk estimates that are very similar to risk estimates using the PHED data. Non-cancer and cancer private/farmer and

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[34] Available: http://www.epa.gov/opp00001/science/handler-exposure-table.pdf
[35] Available: http://www.epa.gov/pesticides/science/handler-exposure-data.html
[36] J. Dawson. Tetrachlorvinphos: Further Revisions to Occupational Risk Assessment for Uses in the Poultry and Cattle Production Industries. 3/28/2002. D281972.
[37] W. Britton. Tetrachlorvinphos: Occupational and Residential Exposure Assessment for Registration Review. 12/21/2015. D426984.

contract/commercial occupational handler risk estimates for exposure scenario 10c are presented separately from the risk summaries for all other occupational handler exposure scenarios in Appendix K: Table K.2 and Appendix L: Tables L.2 and L.4, respectively.

In some cases, due to the lack of data for an exposure scenario or the unique nature of the scenario, surrogate exposure data were used as follows:

- Exposure data for the loading/application of dust formulations were used as a surrogate for the loading/application of wettable powders for rotary and plunger duster applications (10e, 10f). For exposure scenario 10e, exposure data for plunger dusters were used due to the lack of data for the rotary duster application method.
- For the assessment of pet collars as a dust formulation, data for applying dusts using a shaker can were used as a surrogate.
- Unlike more typical exposure scenarios where a RTU paint is only loaded or applied, for TCVP the paint must be mixed/loaded for the liquid (1b), wettable powder (2b), and dust (3a) formulations. These exposure scenarios were assessed using the exposure data appropriate for mixing/loading for each formulation with the exception of dust where WP formulation was used as a surrogate for dust.
- For TCVP applications to livestock with a dust formulation via shaker can, a RTU product is not available; therefore, exposures from the mixing/loading of the dust formulation must be assessed in addition to potential exposure resulting from application via shaker can. As a result, the exposure data for the loading/application via a RTU shaker can was used for the assessment of all scenarios relating to the use. The use of these data results in a more protective assessment than would be if the mixing/loading of the dust were assessed separately.
- Exposures from the application of feed (salt or mineral) blocks in livestock – typically, 5 – 15 per head of cattle or horses – is assumed to be negligible if gloves are worn when placing the blocks. Furthermore, for these products the greater majority of the active ingredient is contained within the block, thus further reducing the exposure potential.

Area Treated or Amount Handled: The following inputs are consistent with those used in the most recently conducted occupational risk assessment for TCVP and, for those inputs relating to the poultry industry, are reflective of research conducted by BEAD at that time.

- Groundboom: 100,000 square feet for applications to poultry buildings
- Backpack and manually pressurized handwand: 20,000 square feet for applications to poultry buildings
- Mechanically pressurized handwand: 100,000 square feet for applications to poultry buildings
- Backpack, handheld/stationary fogger, manually pressurized handwand, mechanically pressurized handwand, rotary spreader: 20,000 birds for direct application to poultry (i.e., approximately 1 square foot/bird)
- Backrubber/facerubber: 50 gallons
- Paint applications: 2 gallons

The following inputs are based on either the most recently conducted permethrin occupational and residential exposure and risk assessment for similar use patterns[38] or best professional judgment of product usage:

- All handheld equipment: 400 animals treated daily
- Handheld/stationary fogger: 100,000 square feet to poultry buildings
- Plunger, shaker can, spoon: 1,000 birds or 1,000 square feet
- Pet collar, pump/trigger spray, and shaker can applications: 8 animals treated daily
- Self-treating dust bags: 10 filled daily (assuming a 12.5 lb dust bag)

The following inputs are consistent with EPA regulatory definitions for large concentrated animal feeding operations (CAFOs)[39]. The inputs assume that a single individual is responsible for the food preparation for the entire CAFO and applies the TCVP feed-through products to the animal feed.

- Cup, pour on: 1,000 cows, 500 horses, and 6,250 pigs for liquid and solid feed-through applications. The number of cows and horses represents the maximum identified for large CAFO operations. The number of pigs was estimated by averaging the maximum number weighing over 55 lbs (2,500) and less than 55 lbs (10,000) in large CAFO operations.

Exposure Duration: Occupational handler exposure is expected to be short- and intermediate-term in duration. Because of the steady state AChE inhibition exhibited by the OPs, steady state exposures (typically 21 days and longer for OPs, but 1 day to reach steady state for tetrachlorvinphos) were assessed and presented for occupational exposures to TCVP products.

Mitigation/Personal Protective Equipment: Estimates of non-cancer inhalation exposure were calculated for various levels of PPE (i.e., respiratory protection). Results are presented for no respirator, PF5 respirator, PF10 respirator, or engineering controls (EC).

The PPE required for occupational use of TCVP varies by formulation type. The respiratory protection required for the occupational handling of TCVP can, at times, differ from label to label with consideration of the same formulation and exposure scenario. Occupational handler exposures are expected from use of TCVP on livestock and pets by livestock handlers, veterinarians, veterinary assistants, and groomers. The pet use formulations include collars, dusts/powders, and pump and trigger sprays. All but one of the TCVP pet product labels do not require PPE, as these are intended for residential sale as well as for occupational use. A summary of PPE required for all TCVP products is presented in Appendix A of D436833.

Days per Year of Exposure: To assess cancer risk, it is assumed that private/farmers would be exposed 10 days per year and commercial applicators would be exposed 30 days per year. The

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[38] C. Smith. Permethrin: Third Revision of the Occupational and Residential Exposure Assessment for the Reregistration Eligibility Decision Document. 4/4/2006. D325428.
[39] http://www.epa.gov/npdes/pubs/sector_table.pdf

term "private/farmer" means that the applicators or one of the workers would apply the pesticides to land owned or operated by the farmer. Commercial applicators mean the applicators are completing multiple applications for multiple clients.

Years per Lifetime of Exposure: It is assumed that handlers would be exposed for 35 years out of a 78-year lifespan.

Lifetime Expectancy: Life expectancy values are from the Exposure Factors Handbook 2011 Edition Table 18-1 (U.S. EPA, 2011). The table shows that the overall life expectancy is 78 years based on life expectancy data from 2007. In 2007, the average life expectancy for males was 75 years and 80 years for females. Based on the available data, the recommended value for use in cancer risk assessments is 78 years.

Occupational Handler Non-Cancer Exposure and Risk Estimate Equations

The algorithms used to estimate non-cancer exposure and dose for occupational handlers can be found in Appendix B of D436833.

Combining Exposures/Risk Estimates

Although occupational dermal and inhalation exposures are anticipated for TCVP, risks have been estimated for inhalation exposures only due to the lack of dermal hazard. Therefore, no combined occupational exposures/risk estimates have been quantified.

Summary of Occupational Handler Non-Cancer Exposure and Risk Estimates

Of the 198 total occupational handler exposure scenarios assessed, the majority (162) are not of concern (i.e., steady state inhalation MOEs are $\geq$ 300) with currently required personal protective equipment (PPE) (i.e., respiratory protection). Of the remaining 36 handler exposure scenarios, 25 are not of concern with consideration of increasing levels of respiratory protection (i.e., 11 occupational handler exposure scenarios result in estimated risks of concern despite the addition of respiratory protection or engineering controls; MOEs at highest level of respiratory protection range from 3.9 to 280). These eleven handler scenarios include dust formulations (mixing/loading/applying TCVP by rotary duster, self-treating dust bag, or shaker can) and wettable powder formulations (mixing/loading/applying TCVP by mechanically-pressurized handgun using MRID 42622301 and mixing/loading/applying using fogging equipment).

A summary of all non-cancer occupational handler exposure scenarios is presented in Appendix K. For risk management purposes, the currently labeled level of respiratory protection and EC has been identified (shaded) for each individual exposure scenario.

Occupational Handler Cancer Exposure and Risk Equations

Cancer risk estimates were calculated using a linear low-dose extrapolation approach in which an LADD is first calculated and then compared with a Q1* that has been calculated for TCVP based on dose response data in the appropriate toxicology study (Q1* = 1.83 x 10^{-3} (mg/kg/day)-1). ADD levels were used as the basis for calculating the LADD values. Dermal and inhalation ADD values were first added together to obtain combined ADD values. LADD values were then calculated and compared to the Q1* to obtain cancer risk estimates. The algorithms used to

estimate the LADD and cancer risk for occupational handlers can be found in Appendix B of D436833.

Summary of Occupational Handler Cancer Exposure and Risk Estimates
Occupational cancer risks were estimated for both private/farmer and contract/commercial handlers. Cancer risks, with currently required PPE, range from 10^{-10} to 10^{-5} for private/farmer handlers and from 10^{-10} to 10^{-4} for contract/commercial handlers with currently required PPE.

Unlike the occupational handler non-cancer risk estimates which were based only on inhalation exposures, the occupational handler cancer risk estimates are quantified based on both dermal and inhalation exposures. This is because, despite the determination of the lack of dermal hazard for TCVP, dermal exposures from TCVP must be quantified for the purpose of cancer risk assessment. As previously described, the PPE required for the occupational use of TCVP varies by formulation type. For example, for feed through (solid and liquid food additives) and feed blocks, occupational handlers are required to wear baseline clothing (i.e., long sleeved shirt, long pants, shoes and socks) and gloves. For all other end-use labels with livestock and outdoor perimeter uses, required PPE can vary dependent on the application type or equipment and can range from baseline clothing and gloves, to the addition of coveralls, or respiratory protection.

A summary of occupational cancer risks as estimated at all levels of personal protection and with use of engineering controls is presented in Appendix L. Tables L.1 and L.2 present cancer risks for private/farmer handlers and Tables L.3 and L.4 risks for contract/commercial handlers. For risk management purposes, the currently labeled level of respiratory protection and EC has been identified (shaded) for each individual exposure scenario.

8.2 Occupational Post-application Exposure/Risk Estimates

HED uses the term post-application to describe exposures that occur when individuals are present in an environment that has been previously treated with a pesticide (also referred to as re-entry exposure). Such exposures may occur when workers enter previously treated areas to perform job functions, including activities related to crop production, such as scouting for pests or harvesting. Post-application exposure levels vary over time and depend on such things as the type of activity, the nature of the crop or target that was treated, the type of pesticide application, and the chemical's degradation properties.

Occupational post-application exposures are not anticipated for TCVP as the majority of application scenarios are not to foliar surfaces. The use of TCVP outdoors as a perimeter treatment is not expected to result in occupational post-application exposure as reentry activities related to crop production (e.g., scouting, harvesting) are not anticipated for this use pattern.

9.0 Public Health and Pesticide Epidemiology Data

Incident Report Memo: D426986, 5/21/15, S. Recore [40]

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[40] S. Recore *et al.*, 5/21/2015, D426986, Tetrachlorvinphos (TCVP): Tier I Review of Human Incidents for Draft Risk Assessment

HED has prepared a Tier I review of human incidents report. For this evaluation, both the OPP Incident Data System (IDS) and the Centers for Disease Control and Prevention/National Institute for Occupational Safety and Health (CDC/NIOSH) Sentinel Event Notification System for Occupational Risk-Pesticides (SENSOR) databases were consulted for pesticide incident data on the active ingredient TCVP. The purpose of the database search is to identify potential patterns in the frequency and severity of the health effects attributed to TCVP exposure.

The Agricultural Health Study (AHS) is a high quality, prospective epidemiology study evaluating the link between pesticide use and various health outcomes including cancer. TCVP is not included in the AHS, and therefore this study does not provide information for this report.

Although there were a moderate number of TCVP incidents reported to Main and Aggregate IDS (n=374) and SENSOR-Pesticides (n=61), most of these incidents were classified as low severity. The effects experienced were generally minimally traumatic and resolving rapidly and usually involve skin, eye or respiratory irritation. Most of the reported incidents were due to handling and applying TCVP products to pets. Based on the low severity of incident cases reported for TCVP in both IDS and NIOSH SENSOR-Pesticides, there does not appear to be a concern at this time that would warrant further investigation. The agency will continue to monitor the incident information and if a concern is triggered, additional analysis will be conducted.

10.0 Cumulative Exposure/Risk Characterization

OPs, like TCVP, share the ability to inhibit AChE through phosphorylation of the serine residue on the enzyme leading to accumulation of acetylcholine and ultimately cholinergic neurotoxicity. This shared MOA/AOP is the basis for the OP common mechanism grouping per OPP's Guidance for Identifying Pesticide Chemicals and Other Substances that have a Common Mechanism of Toxicity (USEPA, 1999). The 2002 and 2006 CRAs used brain AChE inhibition in female rats as the source of dose response data for the relative potency factors and PoDs for each OP, including TCVP. Prior to the completion of Registration Review, OPP will update the OP CRA on AChE inhibition to incorporate new toxicity and exposure information available since 2006.

As described in Section 4.5, OPP has retained the FQPA Safety Factor for OPs, including TCVP, due to uncertainties associated with neurodevelopmental effects in children and exposure to OPs. There is a lack of an established MOA/AOP for the neurodevelopment outcomes which precludes the agency from formally establishing a common mechanism group per the Guidance for Identifying Pesticide Chemicals and Other Substances that have a Common Mechanism of Toxicity (USEPA, 1999) based on that outcome. Moreover, the lack of a recognized MOA/AOP and other uncertainties with exposure assessment in the epidemiology studies prevent the agency from establishing a causal relationship between OP exposure and neurodevelopmental outcomes.

The agency will continue to evaluate the epidemiology studies associated with neurodevelopmental outcomes and OP exposure prior to release of the revised risk assessment. During this period, the agency will determine whether or not it is appropriate to apply the draft guidance document entitled, Pesticide Cumulative Risk Assessment: Framework for Screening Analysis for the neurodevelopment outcomes.

11.0 Appendices

Appendix A. Toxicology Profile
Appendix B. Results for BMD/BMDL modeling for TCVP
Appendix C. Methodologies for HEC Calculations
Appendix D. Physical/Chemical Properties for Tetrachlorvinphos
Appendix E. TCVP and Metabolites
Appendix F. International MRLs and U.S. Tolerances
Appendix G. Summary of Residential Handler Non-Cancer Exposures and Risk Estimates
Appendix H. Summary of Residential Handler Cancer Exposure and Risk Estimates
Appendix I. Summary of Residential Post-Application Non-Cancer Exposure and Risk Estimates
Appendix J. Summary of Residential Post-Application Cancer Exposure and Risk Estimates
Appendix K. Summary of Occupational Handler Non-Cancer Exposures and Risk Estimates
Appendix L. Summary of Occupational Handler Cancer Exposures and Risk Estimates

Appendix A. Toxicology Profile and Executive Summaries

A.1. Toxicology Data Requirements

The requirements (40 CFR 158.500) for the food use for TCVP are in Table A.1. Use of the new guideline numbers does not imply that the new (1998) guideline protocols were used.

Study		Technical	
		Required	Satisfied
870.1100	Acute Oral Toxicity	yes	yes
870.1200	Acute Dermal Toxicity	yes	yes
870.1300	Acute Inhalation Toxicity	yes	yes
870.2400	Primary Eye Irritation	yes	yes
870.2500	Primary Dermal Irritation	yes	yes
870.2600	Dermal Sensitization	yes	yes
870.3100	90-Day Oral Toxicity in Rodents	yes	yes
870.3150	90-Day Oral Toxicity in Non-rodents	yes	yes [a]
870.3200	21/28-Day Dermal	yes	yes
870.3250	90-Day Dermal	no	-
870.3465	90-Day Inhalation	yes	yes [b]
870.3700a	Prenatal Developmental Toxicity in Rodents	yes	yes
870.3700b	Prenatal Developmental Toxicity in Non-rodents	yes	yes
870.3800	Reproduction	yes	yes
870.4100a	Chronic Toxicity in Rodents	yes	yes
870.4100b	Chronic Toxicity in Non-rodents	yes	yes
870.4200a	Carcinogenicity in Rats	yes	yes
870.4200b	Carcinogenicity in Mice	yes	yes
870.4300	Chronic Toxicity/Carcinogenicity in Rats	yes	yes
870.5100	Mutagenicity—Bacterial Reverse Mutation Test	yes	yes
870.5300	Mutagenicity—Mammalian Cell Gene Mutation Test	yes	yes
870.5375	Mutagenicity—Structural Chromosomal Aberrations	yes	yes
870.5xxx	Mutagenicity—Other Genotoxic Effects	yes	no [c]
870.6100a	Acute Delayed Neurotoxicity in Hens	yes	yes
870.6100b	90-Day Neurotoxicity in Hens	yes	yes
870.6200a	Acute Neurotoxicity Screening Battery in Rats	yes	yes
870.6200b	90-Day Neurotoxicity Screening Battery in Rats	yes	yes
870.6300	Develop. Neurotoxicity	yes	yes
870.7485	General Metabolism	yes	yes
870.7600	Dermal Penetration	yes	yes
870.7800	Immunotoxicity	yes	yes
Special Studies	Comparative Cholinesterase in Rats	yes	yes

[a] there is a chronic study; [b] 4-Week study

[c] A follow-up mouse micronucleus assay (OPPTS Harmonized Guideline 870.5395) and a study that investigates possible genotoxic activity in the target organ (liver) are required. This latter study should examine DNA damage potential (Comet assay, DNA adduct formation, or any other DNA target).

A.2 Toxicity Profiles

Table A.2.1 Acute Toxicity of Tetrachlorvinphos Technical

Guideline No.	Study Type	MRID No.	Results	Toxicity Category
870.1100	Acute Oral – Rat	41222504	LD_{50} = 1480 mg/kg (M) 465-965 mg/kg (F)	III
870.1200	Acute Dermal – Rabbit	41222505	LD_{50} > 2000 mg/kg	III
870.1300	Acute Inhalation – Rat	00138933	LC50 > 3.61mg/L	IV
870.2400	Acute Eye Irritation - Rabbit	41222506	moderate	III
870.2500	Acute Dermal Irritation - Rabbit	41222507	slight	IV
870.2600	Skin Sensitization - Guinea Pig	41377902 42981001	sensitizer	N/A
870.6100	Acute Delayed Neurotoxicity	41905901	No clinical signs of neurotoxicity observed (NTE not measured)	N/A

Table A.2.2 Subchronic, Chronic and Other Toxicity Profile of Tetrachlorvinphos (TCVP)

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
870.3100 21-Day Oral Toxicity in (Crl:CD®(SD)IGS BR rats)	45570601 (2001) Acceptable/non-guideline (21-day study; gavage) 0, 8, 12, 20, or 50 mg/kg/day	**Repeat exposure**: Brain ChEI NOAEL = 12 mg/kg/day Brain ChEI LOAEL = 20 mg/kg/day, based on brain cholinesterase activity inhibition in females (day 21). RBC ChEI NOAEL = 8 mg/kg/day RBC ChEI LOAEL = 12 mg/kg/day, based on RBC cholinesterase activity inhibition in males and females ***HIARC: RBC data not reliable*** **Single dose exposure**: RBC ChEI NOAEL = 20 mg/kg. RBC ChEI LOAEL = 50 mg/kg, based on RBC cholinesterase activity in both sexes. NOTE: *HIARC: RBC data not reliable from this study.* Brain ChEI NOAEL =12 mg/kg. Brain ChEI LOAEL = 20 mg/kg, based on brain cholinesterase activity inhibition (ChEI) in males (22%). At 50 mg/kg, males had 54% and females had 23% brain cholinesterase inhibition. $BMDL_{10}$ = 6.7 mg/kg/day BMD_{10} = 9.9 mg/kg/day, based on female RBC ChE inhibition $BMDL_{10}$ = 12.2 mg/kg/day BMD_{10} = 14.7 mg/kg/day, based on female brain ChE inhibition

Table A.2.2 Subchronic, Chronic and Other Toxicity Profile of Tetrachlorvinphos (TCVP)

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
870.3150 90-Day Oral Toxicity (Sprague Dawley rats)	43371201 (1990) Acceptable/guideline 0, 100, 2000, or 5000 ppm (diet) Males: 0, 6.7, 142, and 375 mg/kg/day; Females: 0, 10.0, 197, and 467 mg/kg/day. $BMDL_{10}$ = 8.0 mg/kg/day BMD_{10} = 10.49 mg/kg/day, based on female RBC ChE inhibition	RBC ChEI NOAEL = 6.7 mg/kg/day RBC ChEI LOAEL = 142 mg/kg/day, based on RBC ChEI in both sexes (males 30%*; females 79%**), bilateral basophilic tubules of the kidneys in males, increased fat deposition in the adrenal cortex of females, centrilobular hepatocellular hypertrophy in females and mid-dose males, higher adjusted liver weights (both sexes), higher adjusted adrenal weights in females, and thyroid follicular cell hypertrophy in both sexes. At 467 mg/kg/day, in addition to RBC ChEI in both sexes (males 72%*; females 91%**), females had a 24% brain cholinesterase inhibition, although statistical significance was not attained (females 12%, 14%, 24% brain ChEI with increasing dose; males 1% at HDT). Additionally, decreased body weight was observed throughout the study in males (7%- 12%), with the magnitude of the deficit increasing over time. $BMDL_{10}$ = 8.0 mg/kg/day BMD_{10} = 10.49 mg/kg/day, based on female RBC ChE inhibition $BMDL_{10}$ = 26.3 mg/kg/day BMD_{10} = 61.6 mg/kg/day, based on male RBC ChE inhibition No dose-response for brain ChE inhibition (BMD not run)
870.3200 21/Day Dermal Toxicity (Crl:CD BR Sprague Dawley rat)	41342001 (1989) Acceptable/guideline 0, 10, 100, or 1000 mg/kg/day 6 hours/day, 5 days/week for 15 treatments over a 21-day period	NOAEL = 1000 mg/kg/day LOAEL = not determined. RBC and brain cholinesterase inhibition were not observed in either sex at dose levels up to and including the limit dose. Significant dermal effects were not observed. There were no treatment-related effects on body weight, food consumption, hematology or clinical chemistry parameters (except plasma ChE activity), gross or microscopic pathology in either sex. Plasma ChE inhibition was observed in females at 1000 mg/kg/day.
870.3465 28-Day Inhalation Toxicity (Sprague-Dawley rat)	48803501 (2012) Acceptable/guideline nose-only aerosol 6 hours/day, 5 days/week for 3 weeks at exposure concentrations of 0, 0.05, 0.5, or 1.0 mg/L; during the final week of exposure (week 4), the animals were exposed for 7 days	NOAEL= 0.05 mg/L/day LOAEL = 0.5 mg/L/day, based on an increase in RBC cholinesterase inhibition in both sexes. *Brain cholinesterase activity was not monitored.* Systemic NOAEL not identified. Systemic LOAEL = 0.05 mg/L, based on diffuse adrenal cortical cell vacuolation in both sexes, enlarged adrenals in females, and increased adrenal weights in females. At 0.5 mg/L and 1.0 mg/L, in addition to the adrenal findings, there was a dose-related increase in vacuolation of the ovaries in females, an increase in squamous metaplasia of the larynx in both sexes, and an increase in follicular cell hyperplasia of the thyroids in both sexes.

Sex/Age	Compartment	BMD_{10}	$BMDL_{10}$
Female	RBC	0.394	0.050
Male	RBC	0.122	0.022

Table A.2.2 Subchronic, Chronic and Other Toxicity Profile of Tetrachlorvinphos (TCVP)		
Guideline No./ Study Type	**MRID No. (year)/ Classification /Doses**	**Results**
870.3700a Prenatal developmental in (Sprague Dawley Crl:COBS®CD ® (SD)BR) TXR# 008124, 008616, 018781	40152701 (1987) 41828001(1991) 41967201 (1991) 42520101 (1992) Acceptable/guideline 0 (aqueous 0.5% methyl cellulose), 75, 150, or 300 mg/kg/day GD 6-15; 10 mL/kg (gavage)	**Maternal** NOAEL = 75 mg/kg/day **Maternal** LOAEL = 150 mg/kg/day, based on a reduction in BWG/FC* At 300 mg/kg/day, there were clinical signs of toxicity (tremors and chromodacryorrhea) **Developmental** NOAEL =300 mg/kg/day **Developmental** LOAEL = not identified. *NOTE: Cholinesterase activity was not assessed (RBC, brain).* *BWG not considered an adverse effect since BW was not affected. NOAL/LOAEL should be revised to 150/300 mkd.
870.3700b Prenatal developmental in (New Zealand white rabbit)	00127831 (1982) Acceptable/guideline 0, 150, 375, or 750 mg/kg/day (1% CMC) GD 6-19; 5 mL/kg (gavage)	**Maternal** NOEL = 375 mg/kg/day **Maternal** LOEL = 750 mg/kg/day, based on mortality, abortions, and red vaginal fluid. **Developmental** NOAEL = 375 mg/kg/day **Developmental** LOAEL = 750 mg/kg/day, based on an increase in early resorptions and corresponding increase in post implantation loss, and a decrease in live fetuses/doe. *NOTE: Cholinesterase activity was not assessed (RBC, brain).*
870.3800 Reproduction and Fertility Effects (Charles River CD Crl®SD) BR rats)	42054301 (1991) acceptable/guideline 0, 100, 500, or 2000 ppm (diet) F0 Males 0, 5.2, 26, 102 mg/kg/day F1 Males 0, 6.7, 34, 130 mg/kg/day F0 Females 0, 7.3, 40, or 155 mg/kg/day F1 Females 0, 8.3, 43, or 168 mg/kg/day	**Parental** NOAEL = 500 ppm (males 26/females 40 mg/kg/day) **Parental** LOAEL = 2000 ppm (males 102/females 155 mg/kg/day), based on decreased body weight gain in F1 generation, increased adrenal weights of F0 females, and decreased body weight gains in F0 males. **Offspring** NOAEL = 2000 ppm (males 102/females 155 mg/kg/day) **Offspring** LOAEL was not identified. **Reproductive** NOAEL = 2000 ppm (males 102/females 155 mg/kg/day) **Reproductive** LOAEL was not identified. *NOTE: Cholinesterase activity was not assessed (RBC, brain).*

Table A.2.2 Subchronic, Chronic and Other Toxicity Profile of Tetrachlorvinphos (TCVP)		
Guideline No./ Study Type	**MRID No. (year)/ Classification /Doses**	**Results**
870.4100a Chronic Toxicity (Sprague-Dawley rat)	42980901 (1993) 43335101 (1994) Acceptable/guideline 0, 100, 1000, or 2000 ppm (diet) Males 0, 4.23, 43.2, or 88.5 mg/kg/day Females 0, 5.93, 62.7, or 125.3 mg/kg/day (2-year study)	NOAEL = 100 ppm (4.23/5.93 mg/kg/day) LOAEL = 1000 ppm (43.2/62.7 mg/kg/day), based on histological liver (hypertrophy of periacinar hepatocytes in both sexes and centriacinar degenerative change in males) and adrenal changes (increased incidence of diffuse lipidosis of adrenal zona fasciculata in both sexes); reduced body weight; ~~plasma~~ cholinesterase inhibition in females. RBC cholinesterase inhibition was observed in females at 1000 ppm (29%*) and 2000 ppm (36%**) at week 77/78; 18% and 22% at week 103/104 (not **); brain ChEI in females at 52 and 104 weeks was 17% and 16% (not **). NOAEL = 100 ppm (4.23/5.93 mg/kg/day) LOAEL = 1000 ppm (43.2/62.7 mg/kg/day), based on RBC cholinesterase inhibition in females BMD not run due to lack of dose-response
870.4100b Chronic toxicity (Beagle dog)	42679401 (1993) Acceptable/guideline 0, 0, 6.25, 500, 1000 mg/kg/day; (capsule) 4/sex/group Cholinesterase pre-test, 12, 26, 52 weeks (plasma, RBC) Brain at termination (1 year)	NOAEL = 6.25 mg/kg/day LOAEL = 500 mg/kg/day, based on plasma cholinesterase inhibition (both sexes), decreased red blood cell counts, hemoglobin, hematocrit, MCHC, MCV, alkaline phosphatase, urine specific gravity, and decreased liver and kidney weights. At 1000 mg/kg/day, increased white blood cell counts (females), increased prostate weight, decreased cholesterol (males). RBC and brain cholinesterase inhibition were not observed at any dose level in either sexes.
870.4200a Carcinogenicity (Sprague Dawley rat)	42980901 (1993) 43335101 (1994) acceptable/guideline 0, 100, 1000, or 2000 ppm (diet) Males 0, 4.23, 43.2, or 88.5 mg/kg/day Females 0, 5.93, 62.7, or 125.3 mg/kg/day 104 weeks	NOAEL = 100 ppm (4.23/5.93 mg/kg/day) LOAEL = 1000 ppm (43.2/62.7 mg/kg/day), based on histological liver (hypertrophy of periacinar hepatocytes in both sexes and centriacinar degenerative change in males) and adrenal changes (increased incidence of diffuse lipidosis of adrenal zona fasciculata in both sexes); reduced body weight; cholinesterase inhibition in females. RBC cholinesterase inhibition was observed in females at 1000 ppm (29%*) and 2000 ppm (36%**) at week 77/78; 18% and 22% at week 103/104 (not **); brain ChEI in females at 52 and 104 weeks was 17% and 16% (not **). NOAEL = 100 ppm (4.23/5.93 mg/kg/day) LOAEL = 1000 ppm (43.2/62.7 mg/kg/day), based on RBC cholinesterase inhibition in females BMD not run due to lack of dose-response Increased incidence of thyroid C-cell adenomas in male rats at HDT and adrenal pheochromocytomas in males

Table A.2.2 Subchronic, Chronic and Other Toxicity Profile of Tetrachlorvinphos (TCVP)		
Guideline No./ Study Type	**MRID No. (year)/ Classification /Doses**	**Results**
870.4200b Carcinogenicity (B6C3F1 mouse)	00117443 (1978) Acceptable/guideline 0, 17.5, 64, 320, 1600, 8000, 16000 ppm 0, 2.6, 9.6, 48, 240, 1200, or 2400 mg/kg/day	NOAEL = 1600 ppm (240 mg/kg/day) LOAEL = 8000 ppm (1200 mg/kg/day), based on decreased body weight gain Statistically significant increases in combined hepatocellular adenoma/carcinoma (primarily carcinomas) in female B6C3F1 mice at 1600 ppm. Other doses considered excessive; combined adenomas/carcinomas in males, renal adenomas/carcinomas and combined in males at 16000 ppm
870.4300 Combined Chronic Toxicity/Carcinogenicity (Sprague Dawley rat)	42980901 (1993) 43335101 (1994) acceptable/guideline 0, 100, 1000, or 2000 ppm Males 0, 4.23, 43.2, or 88.5 mg/kg/day Females 0, 5.93, 62.7, or 125.3 mg/kg/day	See above 870.4200a
870.4200a Carcinogenicity (Osborne-Mendel rats)	00117443 () Acceptable/non-guideline 0, 4250, or 8500 ppm for 80 weeks	Statistically significant increase in the incidences of adrenal cortical adenomas and thyroid C-cell adenomas were found in dosed female rats. . High incidences of thyroid C-cell hyperplasia in both sexes further indicated an effect on the thyroid. Study deficiencies (CPRC, 1988); evidence equivocal.
Gene Mutation 870.5100 *Salmonella/Escherichia* bacterial reverse mutation assay	41222508 (1989) Acceptable/ Guideline 66.7, 100, 333, 667, 1000, or 3300 µg/plate in the presence of or 10, 33.3, 66.7, 100, 333, or 667 µg/plate absence of mammalian metabolic activation (S9-mix)	Strains TA98, TA100, TA1535, TA1537, and TA 1538 of *S. typhimurium* were exposed to TCVP from concentrations of 66.7 to 3300 µg/plate in the presence and 10-667 µg/plate absence of mammalian metabolic activation (S9-mix). There was no evidence of induced mutant colonies over background.

Table A.2.2 Subchronic, Chronic and Other Toxicity Profile of Tetrachlorvinphos (TCVP)		
Guideline No./ Study Type	**MRID No. (year)/ Classification /Doses**	**Results**
In vitro mammalian cytogenetics 870.5375 Chinese hamster ovary cells	41312901 (1989) Acceptable/ Guideline Concentrations of 22.9, 44.9, 59.9, 79.8, or 99.8 µg/mL without S9; 12.5, 25, 37,6, or 75.1 µg/mL in the presence of S9-mix.	Positive for inducing chromosomal aberrations at 59.9, 79.8 and 99.8 µg/mL in absence of metabolic activation, but negative at 29.9 or 44.9 µg/mL in absence of metabolic activation. Negative for inducing chromosomal aberrations at 12.5, 25, 37.6, or 75.1 µg/mL in the presence of rat S9 metabolic activation.
Unscheduled DNA Synthesis 870.5550 in mammalian cells in culture	42156401 (1992) Acceptable/ Guideline Doses of 5, 7.5, 10, 15, 20, 23, 25, 27, 30, 35, or 40 µg/mL of TCVP.	Concentrations of 35 and 40 µg/mL were lethal. Results were negative.
870.6100 Acute and 28-Day Delayed Neurotoxicity (Domestic hen)	41905901 (1990) Acceptable/guideline 2500 mg/kg x 2 (21 days apart)	Does not cause delayed neurotoxicity; 4/15 died.
870.6200a Acute Neurotoxicity Screening Battery (Sprague-Dawley Crl:CD®BR rats)	42912501 (1993) Acceptable/guideline 0, 65, 325, or 650 mg/kg (gavage)	NOAEL = 65 mg/kg LOAEL = 325 mg/kg, based on transient neurotoxic effects in both sexes consistent with cholinesterase inhibition. No neuropathological effects. *Cholinesterase activity was not monitored in the study.*
870.6200b Subchronic Neurotoxicity Screening Battery (Crl:CD® BR rats)	43294101 (1994) Acceptable/guideline 0, 200, 1000, or 5000 ppm (diet) (0, 100, 500, or 250 mg/kg/day; standard conversion)	NOAEL = 5000 ppm (250 mg/kg/day); HDT LOAEL = not identified. *Cholinesterase activity was not monitored in the study.*

Table A.2.2 Subchronic, Chronic and Other Toxicity Profile of Tetrachlorvinphos (TCVP)		
Guideline No./ Study Type	**MRID No. (year)/ Classification /Doses**	**Results**
870.6300 Developmental Neurotoxicity (Crl: CD® (SD)IGS BR VAF/Plus® rats)	46660601 (2005) acceptable/guideline 0, 10, 50, or 200 mg/kg/day GD 6 –LD 6 (gavage) 46791401 (2006) +control data	**Maternal** NOAEL = 200 mg/kg/day LOAEL = not identified. **Offspring** NOAEL = 50 mg/kg/day LOAEL = 200 mg/kg/day, based on deceased body weight, body weight gain, several morphometric linear brain measurements in both sexes, and decreased absolute brain weight in males on PND 70 *Cholinesterase activity was not monitored in the study.*
870.7485 Metabolism and Pharmacokinetics (Sprague-Dawley CD rat)	MRID 41988401 (1991) Acceptable/guideline 5 mg/kg [single and repeat (14 days)] and 250 mg/kg (single)	Most of radioactivity recovered in urine (46%-60%) and feces (38%-56%) within 48 hours post dose; major metabolite in urine was trichloromandelic acid (18%-26%); major metabolite in feces was trichlorophenylethanol (>13%). Since the oral LD50 for female rats is lower than the male LD50, it is noteworthy that males of all groups excreted more total label as trichloromandelic acid, a more completely metabolized form of TCVP; high-dose females tended to excrete more of the label as desmethyl TCVP (with the phosphate group still attached to the remainder of the molecule), a compound that could be derived from TCVP with only a single metabolic step.
870.7600 Dermal Penetration (Sprague Dawley CD rats)	MRID 42111501 (1991) MRID 41862401 (1991) Acceptable/Guideline 0, 0.01, 0.1, 1, or 5 mg/cm^2 for exposures of 0.5, 1, 2, 4, and 10 hours and 10 hour wash with 72 hour exposure	Absorbed dose following 0.01 mg/cm^2 dose is 9.57% following 10-hour exposure.
870.7800 Immunotoxicity (Crl:CD-1(ICR) female mouse)	48794701 (2012) acceptable/guideline 0, 75, 300, 1200 mg/kg/day	Systemic NOAEL = 1200 mg/kg/day, Systemic LOAEL = not identified. Immunotoxicity NOAEL = 1200 mg/kg/day. Immunotoxicity LOAEL = not identified.

Table A.2.2 Subchronic, Chronic and Other Toxicity Profile of Tetrachlorvinphos (TCVP)		
Guideline No./ Study Type	**MRID No. (year)/ Classification /Doses**	**Results**
Special study Comparative cholinesterase *gestational CCA* (Crl:CD(SD)IGS BR VAF/Plus rats)	MRID 48291101 (2010) Acceptable/non-guideline 1% aqueous (w/v) methylcellulose 0, 75, 150, 300 mg/kg/day GD 6-21 (gavage)	The main purpose of this study was to determine whether there is differential sensitivity between dams and fetuses with respect to cholinesterase inhibition following oral exposure to TCVP. ***RBC ChE***: Neither the dams nor the fetuses demonstrated RBC ChE inhibition at dose levels where RBC ChE inhibition (ChEI) would be expected. The repeat dosing study (2012, 48773401) conducted in the same laboratory in the same strain of rat clearly demonstrated RBC ChE inhibition at 50 and 200 mg/kg/day in female rats. In the gestational/fetal study, RBC results in the dams were ↓5.1%, ↓15%, and ↓3% RBC ChEI, with increasing dose. The fetal RBC data were of little value because only one or two fetal samples were available for the control, low, and high dose groups and no sample was available for the mid dose group. *There was no way to compare adult and fetal RBC ChE.*activity ***Brain ChE.*** Brain ChE inhibition was dose dependent in dams (↓31%, ↓44% and ↓67% with increasing dose). Fetal brain ChE values (↓20%, ↓20.9% and ↓20.8%, with increasing dose) showed no dose-response and are questionable. However, the data suggest that the fetal brain ChE is not more sensitive to inhibition by TCVP than the dams. ***Plasma ChE***. Plasma ChE inhibition in dams was dose dependent ↓62%, ↓71% and ↓77%, with increasing dose). Fetal plasma ChE values were ↓22%, ↓18.5% and ↓20.8%, with increasing dose. The lack of a dose response raises questions as to whether these lower values are actually inhibition. However, the data do not indicate that the fetuses are more sensitive than the dams. ***Classification:*** This *in vivo* comparative ChE study is classified as **Acceptable/non-guideline**. The inability of the laboratory to detect RBC ChE in the dams and the flat dose response curves for the brain ChE in both pups and adults confounds the interpretation of the study. However, no additional gestational CCA study is being requested at this time because there is no indication that the fetuses were more sensitive than the dams.

Table A.2.2 Subchronic, Chronic and Other Toxicity Profile of Tetrachlorvinphos (TCVP)

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
Special studies Comparative cholinesterase *Acute CCA* (Crl:CD(SD)IGS BR VAF/Plus strain rat)	MRID 48294601 (2010) Acceptable/non-guideline Single gavage dose (1% aqueous methylcellulose) young adult, PND 11, PND 21 0, 75, 150 or 300 mg/kg	The main purpose of this study was to determine whether there is differential sensitivity among the PND11, PND21 and adults with respect to cholinesterase inhibition following exposure to TCVP. Overall, there is little confidence in the ChE data mainly because of the lack of clear dose and temporal responses. The number of samples in many cases was inadequate due to sample loss (no sample available, 1, 2, or 3 samples). Also, duplicate samples that did not replicate contributed to the low number of samples available for a meaningful assessment. Brain ChE assessment also appeared to be affected by the low number of samples. The results for all three enzyme sources indicated that there was inhibition at all doses but there was poor dose response with the degree of apparent inhibition at the higher doses often less that at the low dose of 75 mg/kg/day. There was also a lack of temporal concordance with high apparent inhibition at one time, a much lower degree at the following time point, and back to the higher level at the next time point. Further, there was more or similar apparent inhibition at the low dose of 75mg/kg in this acute study than there was in the repeat dosing study (2012, MRID 48773401, eleven daily doses) at 200 mg/kg/day and in the gestational study (2010, MRID 48291101, fifteen daily doses). It is noted that the repeat dosing study indicated that there was no increase in sensitivity of the pups relative to the adults with regard to ChEI by TCVP. However, in this acute study, there were several comparisons among the PND11, PND21 and adults that suggested the pups were more sensitive. Although there is little confidence in the ChEI data in this study, no additional acute CCA study is being requested at this time. ***Benchmark Dose (BMD) modeling.*** BMD modeling was performed but could not be done with the RBC data or for the PND11 brain data because of too few samples and/or the data would not otherwise fit the models. BMD modeling for the brain ChE data (3-hour time point) indicated that for males, the adults were slightly more sensitive than the PND 21 pups but the females were considered similar with respect to the BMD_{10} and $BMDL_{10}$.

TCVP/Study	Sex/Age	Compartment	BMD Results (mg/kg/day)	
			BMD_{10}	$BMDL_{10}$
MRID 48294601 Acute CCA	Adult male	Brain	6.76716	5.02249
MRID 48294601 Acute CCA	Adult female	Brain	11.2932	4.55107
MRID 48294601 Acute CCA	Male pup PND 21	RBC	16.8647	9.71265
MRID 48294601 Acute CCA	Female pup PND 21	Brain	9.80073	4.6942
MRID 48294601 Acute CCA	Male pup PND 21	Brain	11.246	6.76389

This study is classified as **Acceptable/Non-Guideline.** There is too much variability in the ChE data to make meaningful comparisons for sensitivity for RBC and brain ChE inhibition. Although there is little confidence in the ChEI data in this study, no additional acute CCA study is being requested at this time. **UPDATE: another acute CCA study report was identified (MRID 48773401a); see below.**

Table A.2.2 Subchronic, Chronic and Other Toxicity Profile of Tetrachlorvinphos (TCVP)

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
Special studies Comparative cholinesterase acute CCA (Crl:CD(SD)IGS BR VAF/Plus strain	48773401a (2012) Acceptable/Non-guideline. 0, 5, 10, 50 or 200 mg/kg/day single gavage dose (1% aqueous methylcellulose; 10 mL/kg) young adult, PND 11 pups, PND 21 pups	The NOAEL for adult rats (both sexes) for RBC and brain cholinesterase inhibition following an acute oral dose was not determined. The LOAEL for adult rats is 10 mg/kg. The NOAEL for PND 21 pups could not be determined, based on RBC and brain cholinesterase inhibition at all dose levels following acute oral exposure. The LOAEL for PND 11 pups is 10 mg/kg. The NOAEL for PND 11 pups could not be determined, based on RBC and brain cholinesterase inhibition at all dose levels following acute oral exposure. The LOAEL for PND 11 pups is 10 mg/kg.

TCVP/Study	Sex/Age	Compartment	BMD Results (mg/kg)	
			BMD_{10}	$BMDL_{10}$
MRID 48773401a Acute CCA	Male PND11	Brain	5.1	4.5
	Female PND11	Brain	5.9	4.8
MRID 48773401a Acute CCA	Male PND11	RBC	5.0	4.1
	Female PND11	RBC	3.4	2.8
MRID 48773401a Acute CCA	Male PND21	Brain	3.5	3.2
	Female PND21	Brain	5.3	3.7
MRID 48773401a Acute CCA	Male PND21	RBC	3.2	2.8
	Female PND21	RBC	4.6	2.8
MRID 48773401a Acute CCA	Male Adult	Brain	7.4	5.6
	Female Adult	Brain	11.6	9.8
MRID 48773401a Acute CCA	Male Adult	RBC	6.5	3.6
	Female Adult	RBC	14.9	11.2

<table>
<tr>
<td>Special studies
Comparative cholinesterase

repeat CCA

(Crl:CD(SD)IGS BR VAF/Plus strain rat)</td>
<td>48773401 (2012)
Acceptable/Non-guideline.
0, 5, 10, 50 or 200 mg/kg/day for both ages.</td>
<td>
The main purpose of this study was to determine whether there is differential sensitivity between young adults and PND 11 pups with respect to cholinesterase inhibition following repeat oral exposure (11 doses) to TCVP.

Table 1 shows the adult ChEI data (3 hours after last dose) and Table 2 shows the pup ChEI data. There was a dose-related reduction in RBC and brain cholinesterase activity in both sexes and both age groups
<table>
<tr><th colspan="3">Table 1. Inhibition (%) of RBC and Brain ChE Activity in Adult Rats (repeat)</th></tr>
<tr><th>Dose (mg/kg/day)</th><th>Males</th><th>Females</th></tr>
<tr><td colspan="3">RBC</td></tr>
<tr><td>5</td><td>12%</td><td>8%</td></tr>
<tr><td>10</td><td>13%*</td><td>8.7%</td></tr>
<tr><td>50</td><td>30%**</td><td>40%**</td></tr>
<tr><td>200</td><td>36%**</td><td>62%**</td></tr>
<tr><td colspan="3">Brain</td></tr>
<tr><td>5</td><td>2%</td><td>-</td></tr>
<tr><td>10</td><td>7%</td><td>12%*</td></tr>
<tr><td>50</td><td>14.9%**</td><td>42%**</td></tr>
<tr><td>200</td><td>17.8%**</td><td>57%**</td></tr>
</table>
<table>
<tr><th colspan="3">Table 2. Inhibition (%) of RBC and Brain ChE Activity in Pups (repeat)</th></tr>
<tr><th>Dose (mg/kg/day)</th><th>Males</th><th>Females</th></tr>
<tr><td colspan="3">RBC</td></tr>
<tr><td>5</td><td>2%</td><td>-</td></tr>
<tr><td>10</td><td>2%</td><td>-</td></tr>
<tr><td>50</td><td>33%**</td><td>19%**</td></tr>
<tr><td>200</td><td>60%**</td><td>62%</td></tr>
<tr><td colspan="3">Brain</td></tr>
<tr><td>5</td><td>4%</td><td>4%</td></tr>
<tr><td>10</td><td>6%</td><td>6%</td></tr>
<tr><td>50</td><td>16%**</td><td>18.7%**</td></tr>
<tr><td>200</td><td>46%**</td><td>45%**</td></tr>
</table>
RBC ChE inhibition. At 50 mg/kg/day, both male pups and male adults had similar levels of inhibition (30% to 33%), whereas at 200 mg/kg/day, the male pups were inhibited to ≈60% compared to 36% in the male adult rats. At 50 mg/kg/day, adult females demonstrated more inhibition (≈40%) than the female pups (19%) but at 200 mg/kg/day, both female pups and female adults had ~62% inhibition.
Brain ChE inhibition. Adult females displayed greater brain ChE inhibition at all dose levels than the adult males, whereas a similar magnitude of brain ChE inhibition was observed in male and female pups. Adult females displayed brain ChE inhibition at all dose levels.
A benchmark dose analysis of the cholinesterase data (RBC and brain) was performed that provides both the BMD_{10} and $BMDL_{10}$ of adults and PND11 pups.
<table>
<tr><th colspan="5">BMD_{10}s and $BMDL_{10}$s for Adult Rat and PND 11 Pup Cholinesterase</th></tr>
<tr><th></th><th>RBC BMD_{10}</th><th>RBC $BMDL_{10}$</th><th>Brain BMD_{10}</th><th>Brain $BMDL_{10}$</th></tr>
<tr><td>Adult ♂</td><td>7.7178</td><td>3.5942</td><td>33.803</td><td>24.4489</td></tr>
<tr><td>Adult ♀</td><td>8.6762</td><td>6.1335</td><td>7.1764</td><td>5.4980</td></tr>
<tr><td>PND 11 ♂</td><td>20.4688</td><td>15.9719</td><td>33.4825</td><td>26.5707</td></tr>
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</tr>
</table>

Table A.2.2 Subchronic, Chronic and Other Toxicity Profile of Tetrachlorvinphos (TCVP)		
Guideline No./ Study Type	**MRID No. (year)/ Classification /Doses**	**Results**
		PND 11 ♂ | 20.5608 | 13.1692 | 24.2224 | 18.9412 *Overall conclusion.* The main objective of this study was to determine if the pups are more sensitive than the adults to the inhibitory potential of TCVP. Based on assignment of the NOAEL and LOAEL and the BMD modeling, there was no demonstration for increased sensitivity of the pups relative to the adults for either RBC or brain ChE. It is noted, however, that the magnitude of the high dose male pup brain and RBC ChE inhibition is greater than that in the adult males, but the significance is not established.

A.3 Hazard Identification and Endpoint Selection

A.3.1 Acute Dietary Reference Dose (aRfD) – All Populations

Study Selected: Acute Comparative Cholinesterase Study - Rats
MRID No.: 49773401a
Dose and Endpoint for Risk Assessment: A $BMDL_{10}$ of 2.8 mg/kg associated with RBC ChE inhibition in male PND 21 pups was selected as a suitable PoD for the acute dietary (all populations) exposure scenario. The corresponding BMD_{10} was 3.2 mg/kg/day.
Comments about Study/Endpoint/Uncertainty Factors: Data from the young rat from the acute CCA study are appropriate for acute POD derivation, since effects were observed after a single exposure and the endpoint is the most sensitive adverse response in all populations. The study provides the lowest POD following a single dose. A UF of 1000X (10X to account for interspecies extrapolation, 10X for intraspecies variation, and 10X for the FQPA safety factor (incorporating uncertainty in the human dose-response relationship for neurodevelopmental effects (see Section 4.5)) results in an aPAD of 0.0028 mg/kg/day; the (FQPA) factor may be excluded for the sub-population of adults 50-99 (aPAD of 0.028 mg/kg/day).

A.3.2 Steady State Reference Dose (ssRfD) –All Populations

Study Selected: Acute Comparative Cholinesterase Study - Rats
MRID No.: 49773401a
Dose and Endpoint for Risk Assessment: A $BMDL_{10}$ of 2.8 mg/kg/day associated with RBC ChE inhibition in male PND 21 pups was selected as a suitable PoD for the acute dietary (all populations) exposure scenario. The corresponding BMD_{10} was 3.2 mg/kg/day.
Comments about Study/Endpoint/Uncertainty Factors: Although the steady state dietary endpoint was selected from an acute dose comparative cholinesterase study, the duration of this study is considered appropriate for this exposure scenario since AChE data across the TCVP database demonstrate that there is no progression of AChE inhibition over exposure duration, and steady state inhibition occurs essentially after a single dose. A longer-term exposure does not result in a lower POD, as evidenced by the larger BMD_{10}s found for the repeat dose CCA data.

The point of departure is protective of any exposure duration longer than 21-days, including chronic exposure, since cholinesterase inhibition does not increase after reaching maximum inhibition or steady state and occurs following one exposure to TCVP. A UF of 1000X (10X to account for interspecies extrapolation, 10X for intraspecies variation, and 10X for the FQPA safety factor (incorporating uncertainty in the human dose-response relationship for neurodevelopmental effects (see Section 4.5)) results in an ssPAD of 0.0028 mg/kg/day; the (FQPA) factor may be excluded for the sub-population of adults 50-99 (ssPAD of 0.028 mg/kg/day).

A.3.4 Incidental Oral Exposure (Steady-State)

Study Selected: Acute Comparative Cholinesterase Study - Rats
MRID No.: 49773401a
Dose and Endpoint for Risk Assessment: A $BMDL_{10}$ of 2.8 mg/kg associated with RBC ChE inhibition in male PND 21 pups was selected as a suitable PoD for the acute dietary (all populations) exposure scenario. The corresponding BMD_{10} was 3.2 mg/kg/day.
Comments about Study/Endpoint/Uncertainty Factors: Data from the young rat from the acute CCA study are appropriate for the incidental oral assessment since the AChE data across the TCVP database demonstrate that there is no progression of AChE inhibition over exposure duration, and steady state inhibition occurs essentially after a single dose, and the endpoint is the most sensitive adverse response in all populations. A UF of 1000X (10X to account for interspecies extrapolation, 10X for intraspecies variation, and 10X for the FQPA safety factor (incorporating uncertainty in the human dose-response relationship for neurodevelopmental effects (see Section 4.5)) is appropriate for incidental oral exposures.

A.3.6 Dermal Exposure

There is no potential hazard *via* the dermal route, based on the lack of treatment-related effects, including the lack of RBC and brain cholinesterase inhibition following repeat dermal exposure of rats at dose levels up to 1000 mg/kg/day, and there is no concern for quantitative susceptibility.

A.3.7 Inhalation Exposure (Steady State)

Study Selected: 28-day Inhalation Toxicity Study
MRID No.: 48803501
Dose and Endpoint for Risk Assessment: A $BMDL_{10}$ of 0.02 mg/L/day associated with RBC ChE inhibition in both sexes, following inhalation exposure, was selected as a suitable POD for assessing the potential risk associated with inhalation exposure (single day and steady-state). The corresponding BMD_{10} was 0.12 mg/L/day.

Comments about Study/Endpoint/Uncertainty Factors: A route-specific, 28-day inhalation toxicity study was used for the steady-state inhalation assessment. Using the Agency's Reference concentration (RfC) methodology, human equivalent concentrations (HECs) and Human

Equivalent Doses (HEDs) was calculated for residential and occupational handlers. Since the inhalation POD is based on a route-specific toxicity study, no absorption factor is necessary to estimate exposure. The standard interspecies extrapolation uncertainty factor can be reduced from 10X to 3X due to the HEC calculation accounting for pharmacokinetic (not pharmacodynamic) interspecies differences. The intraspecies uncertainty factor remains at 10X.

A total uncertainty factor of 30X is appropriate for inhalation exposures [3X for interspecies extrapolation, 10X for intraspecies variation] for adult males and females 49+. The FQPA safety factor (10X) will be retained for infants, children, youths, and women of child-bearing age for all exposure scenarios to account for uncertainties introduced by the lack of sufficient data to quantify potential neurodevelopmental effects observed in epidemiology data on the OP, chlorpyrifos.

A.4 Executive Summaries

A.4.1 Subchronic Toxicity

870.3100 90-Day Oral Toxicity – Rat

In a subchronic oral toxicity study (MRID 43371201), tetrachlorvinphos (TCVP; 99% a.i.; Batch KMJ 012) was given to Sprague Dawley rats (10/sex/group) in the diet at doses of 0, 100, 2000, or 5000 ppm (0, 6.7, 142, and 375 mg/kg/day for males; 0, 10.0, 197, and 467 mg/kg/day for females) for 13 weeks.

Survival was not adversely affected in either sex, and there were no clinical signs of toxicity. There were no effects on body weight in the females, but decreased body weight (7%-12%) was observed in males at 5000 ppm throughout the study.

Red blood cell (RBC) cholinesterase (ChE) inhibition was observed in males at 2000 ppm (30%) and 5000 ppm (72%) and in females at 2000 ppm (79%) and 5000 ppm (91%). A noteworthy finding was that 2 rats/sex at 5000 ppm had no measurable RBC ChE activity at 13 weeks. Brain cholinesterase inhibition was observed in females at all dose levels (12%, 14%, 24%, with increasing dose), but statistical significance was not attained at any dose level. Brain cholinesterase inhibition was not observed in males.

Liver weight was increased in females at 2000 ppm (22% when adjusted for body weight) and at 5000 ppm 22%-28%, actual and adjusted). Males displayed an increase in adjusted liver weight (8% and 19% at 2000 ppm and 5000 ppm, respectively). Increased kidney weights were observed in males at 5000 ppm (18% adjusted for body weight), and increased adrenal weights (actual/adjusted) were observed in females at 2000 ppm (20%/28%) and 5000 ppm (28%/32%). There was a dose-related increase in the incidence and severity of bilateral basophilic tubules of the kidneys in males and in the incidence of cellular alteration (fat deposition) in the adrenal cortex of females at 2000 ppm (7/10) and 5000 ppm (9/10). All females at 2000 ppm and 5000 ppm displayed centrilobular hepatocellular hypertrophy, with the severity increasing with dose. In males, the incidence of hepatocellular hypertrophy was significantly increased at 2000 ppm (8/10),

with 2 displaying general cell enlargement, whereas only 1/10 males at 5000 ppm displayed hepatocellular hypertrophy and 7/10 displayed general cell enlargement in the liver. There was a dose-related increase in the incidence of thyroid follicular cell hypertrophy in both sexes.

The NOAEL is 6.7 mg/kg/day, based on RBC ChEI in both sexes (males 30%*; females 79%**), bilateral basophilic tubules of the kidneys in males, increased fat deposition in the adrenal cortex of females, centrilobular hepatocellular hypertrophy in females, higher adjusted liver weights (both sexes), higher adjusted adrenal weights in females, and thyroid follicular cell hypertrophy in both sexes at the LOAEL of 142 mg/kg/day. At 467 mg/kg/day, decreased body weight was observed throughout the study in males (7%- 12%), with the magnitude of the deficit increasing over time, females had a 24% brain cholinesterase activity inhibition, although statistical significance was not attained (females 12%, 14%, 24% brain ChEI with increasing dose; males 1% at HDT), and both sexes displayed RBC ChEI (males 72%; females 91%).

This study is classified as Acceptable/Guideline, and it satisfies the guideline requirement (OCSPP 870.3100; OECD 408) for a subchronic oral toxicity study in the rat.

Single Day and 21-Day Oral Toxicity – Rat

In a 21-day oral toxicity study (MRID 45570601), tetrachlorvinphos (99.1% a.i., lot #801066) was administered to 18 Crl:CD®(SD)IGS BR rats/sex/dose by gavage at dose levels of 0, 8, 12, 20, or 50 mg/kg/day. Seven or eight animals/sex/group were ***sacrificed approximately 3.5 hours following the first dose*** (time to peak effect); the remaining 10/sex/group were killed after an additional 21 days of dosing. Blood samples were taken for plasma and RBC cholinesterase (ChE) determinations approximately one week prior to study initiation, 3.5 hours following dosing on the first day (day 0), on study days 1, 7, and 14, and at study termination (day 21). Whole brain ChE levels were measured after sacrifice on days 0 and 21.

No treatment-related clinical signs of toxicity or deaths were observed in any animal during daily observations or 1 hour post-dosing. Body weights were similar between the treated and control groups throughout the study.

Dose-related inhibition of ChE activity was observed following both acute and repeated exposures. Inhibition in females occurred at a lower dose than in males. Following a single dose of 50 mg/kg, inhibition of plasma ChE activities (63-67%) relative to concurrent controls were observed in males and females. Also significant inhibition (37-46%) of plasma ChE activities were observed in males and females at 20 mg/kg and in females at 12 mg/kg. However, the LOAEL for plasma ChE inhibition was 8 mg/kg based on inhibition of plasma ChE activity relative to pretest values in males. The NOAEL for plasma ChE inhibition was not established. Significant inhibition (37-46%) of RBC ChE activities from both sexes were observed at 50 mg/kg only. Significant inhibition of whole brain ChE was observed n males at 50 mg/kg (54%) and 20 mg/kg (22%) and in females at 50 mg/kg (23%).

Following repeated exposure, plasma ChE activity in the 20- and 50-mg/kg/day males was similar to the concurrent control levels at each time point with the exception of the high-dose males on day 1 (25% inhibition). However in females, plasma ChE activity was significantly inhibited by 26-30% in the 8-mg/kg/day group beginning on day 14 and by 23-67% in the 12-, 20- and 50-mg/kg/day groups beginning on day 1. Inhibition of RBC ChE levels in 50-mg/kg/day males and females was transient with a maximum inhibition at day 7 (44% and 57%, respectively) followed by modest recovery in males and slight recovery in females. Whole brain ChE activity in males was not affected by repeated exposure. In contrast, significant inhibition of brain ChE activities were observed in the 50 mg/kg/day (36%) and 20 mg/kg/day (16%) females.

Following both a single and 21-day repeated dose of tetrachlorvinphos, the LOAEL for brain ChE inhibition was 20 mg/kg, based on inhibition of brain ChE activity in males with a NOAEL of 12 mg/kg.

Following a single dose of tetrachlorvinphos, the LOAEL for erythrocyte ChE inhibition was 50 mg/kg, based on inhibition of erythrocyte ChE activity with a NOAEL of 20 mg/kg. Because reproducibility of ChE activity of the rat RBC samples was poor and the standard deviations were large for all groups, the RBC ChE inhibition measurements in the 21-day toxicity study were judged to be unreliable. Therefore, the HIARC (TXR# 0050548; dated March 7, 2002) concluded not to use RBC ChE data from this 21-day study due to lack of confidence in the results.

Following single and repeated exposure to tetrachlorvinphos, the LOAEL for plasma ChE inhibition was 8 mg/kg, based on inhibition of plasma ChE activity relative to pretest values in males. The NOAEL for plasma ChE inhibition was not established.

This study is classified as Acceptable/non-Guideline, and it does not satisfy any guideline requirement.

870.3150 90-Day Oral Toxicity - Dog

No subchronic study.

870.3200 21/28-Day Dermal Toxicity - Rat

In a repeat dose dermal toxicity study (MRID 41342001), male and female Crl:CD BR rats (5/sex/dose) received dermal applications of 0, 10, 100, or 1000 mg/kg/day Rabon Technical (TCVP; 99% a.i.;) moistened with deionized water for 6 hours/day, 5 days/week for a total of 15 treatments over a 21-day period.

Rabon Technical did not induce significant dermal effects at dose levels up to and including 1000 mg/kg/day. Treatment caused a statistically significant decrease in plasma cholinesterase activity in females at 1000 mg/kg/day. Plasma cholinesterase was also lower than control values for males at the mid and high doses and females at the mid dose; these differences were not statistically significant. TCVP did not result in brain or RBC AChE inhibition, and there were no adverse effects on mortality, body weight, food consumption, hematology, clinical chemistry, organ

weights, or gross and histopathology. The NOAEL is established at 1000 mg/kg/day (the limit dose), since plasma cholinesterase inhibition is not considered a relevant adverse endpoint.

This study is classified as Acceptable/non-Guideline. The study does not satisfy the guideline requirement (OCSPP 870.3200) for a repeat dose dermal toxicity study since an inadequate number of animals per dose were tested; however, the study is adequate for the determination that a dermal risk assessment is not required for TCVP.

870.3465 Subchronic Inhalation – Rat

In a nose-only inhalation toxicity study (MRID 48803501), tetrachlorvinphos (TCVP; Lot No. TX 100113; 100% purity) aerosol was administered to male and female Sprague-Dawley rats (10/sex/concentration) for 6 hours/day, 5 days/week for 3 weeks at exposure concentrations of 0, 0.05, 0.5, or 1.0 mg/L. During the final week of exposure (week 4), the animals were exposed for 7 days. An additional 10 rats/sex/concentration were included in the control and high dose groups and sacrificed 14 days after completion of the 28-day exposure period to determine the reversibility of any effects observed. Actual exposure concentrations as measured by HPLC were 100%, 100%, and101% of target values. The mass median aerodynamic diameters (MMADs) ± geometric standard deviations (GSD) were 2.57 µm ±3.785, 4.51 µm ±3.541, and 4.27 µm ±3.343 for the low-, mid- and high concentrations, respectively.

There were no treatment-related deaths. Treatment-related reduced body weights (↓7%* and ↓8%**) and body weight gains (↓27%** and ↓34%***) were observed in males from the mid- and high exposure groups, respectively. The body weight difference persisted through the recovery period in the high-exposure (↓12%) male recovery group, but the weight gain during those 2 weeks was slightly higher (5%) relative to the control group. Bodyweight was comparable among the female groups throughout the study. Body weight gain was reduced in mid- (↓23%) and high (↓32%) exposure females, but body weight gain was comparable to the control during the recovery period. Food consumption was decreased throughout the study in the mid- and high male groups and during the first two weeks in the low dose male group, whereas food consumption was comparable among the female groups. There were no treatment-related findings during the ophthalmoscopic examinations. Decreased hemoglobin concentration and increased platelets were noted in high exposure concentration females, but these findings were no longer evident at the end of the 2-week recovery period. Calcium was slightly, but significantly, elevated in males at all three exposure levels, but there was no dose-response. Cholesterol was significantly elevated in females from the mid- (↑22%) and high (↑27%) exposure groups. These findings were not observed in the recovery group.

Statistically significant RBC ChE activity inhibition ($p<0.001$) was observed in females at the mid- and high exposure concentrations (35% and 30%, respectively). Statistically significant AChE and RBC ChE activity inhibition ($p<0.001$) was observed in males at the mid- and high exposure concentrations (38% and 31% for AChE, respectively; 24% and 31% for RBC ChE, respectively). Plasma acetylcholinesterase activity (58% to 70%) and plasma butyrylcholinesterase activity (66% to 87%) were decreased relative to controls at all exposure

concentrations in females. All cholinesterase activities were lower relative to controls in the male and female recovery groups, but the differences were not statistically significant.

Treatment-related gross findings were limited to discoloration and enlargement of the adrenal glands at the mid- and high exposure concentrations in males, and in females at all exposure concentrations. Diffuse adrenal cortical cell vacuolation (minimal to moderate with an exposure-related incidence) was observed in both males and females at all exposure concentrations. Minimal follicular cell hypertrophy of the thyroid gland was observed with an exposure-related incidence in both sexes at the mid- and high exposure concentrations. Minimal to mild ovarian interstitial cell vacuolation was observed with an exposure-related incidence in females at the mid- and high exposure concentrations. The findings in the thyroid and ovary were referred to as "commonly observed in this strain and age of rat," but no historical control data or literature citations were provided. In the recovery group, 2/5 males and 2/5 females at the high dose had minimal diffuse adrenal cortical cell vacuolation (0/5 incidence in recovery controls). No other treatment-related microscopic findings were observed in the recovery group.

Based on the effects seen in this study, a systemic NOAEL in male and female Sprague-Dawley rats was not identified. The systemic LOAEL in male and female rats was 0.05 mg/L, based on diffuse adrenal cortical cell vacuolation in both sexes, enlarged adrenals in females, and increased adrenal weights in females. At 0.5 mg/L and 1.0 mg/L, in addition to the adrenal findings, there was a dose-related increase in vacuolation of the ovaries in females, an increase in squamous metaplasia of the larynx in both sexes, and an increase in follicular cell hyperplasia of the thyroids in both sexes.

The NOAEL for cholinesterase inhibition was 0.05 mg/L, based on an increase in RBC cholinesterase inhibition in both sexes at 0.5 mg/L/day. Brain cholinesterase activity was not monitored.

The RBC cholinesterase data from this study have been evaluated using benchmark dose modeling techniques. The results are shown below.

BMD_{10}/$BMDL_{10}$ Results (mg/L)			
Sex/Age	**Compartment**	**BMD_{10}**	**$BMDL_{10}$**
Female	RBC	0.394	0.050
Male	RBC	0.122	0.022

This inhalation toxicity study is classified as **Acceptable (Guideline)** and satisfies the guideline requirement for a repeat dose inhalation toxicity study.

COMMENT: Although a no effect dose was not identified for the findings in the adrenal (LOAEL 8.7 mg/kg/day), when compared on a mg/kg/day basis to the $BMDL_{10}$ (95% lower confidence limit on the BMD_{10}) established for cholinesterase inhibition, the point of departure

(POD; 1.31 mg/kg/day) used in the inhalation exposure risk assessment is protective of these adrenal findings.

A.4.2 Prenatal Developmental Toxicity

870.3700a Prenatal Developmental Toxicity Study – Rat

In a developmental toxicity study (MRID 40152701), tetrachlorvinphos (98.6% ai; Lot No. 10-56-0-0) was administered *via* gavage to groups of 25 Sprague-Dawley Crl:COBS®CD®(SD)BR pregnant rats/groups at dose levels of 0 (0.5% methyl cellulose), 75, 150, or 300 mg/kg/day from gestation day (GD) 6 through GD 15.

All dams survived until study termination. At 300 mg/kg/day, one dam displayed tremors from day 10 onward, and chromodacryorrhea was observed only at this dose level. Although body weights were comparable among the groups, body weight gains were significantly reduced at 300 mg/kg/day throughout the dosing period (52%), and food consumption was also reduced. The numbers of corpora lutea, implantations, resorptions, and dams with liable fetuses were comparable among the groups. The mean number of live fetuses, sex ratio, and fetal body weights were comparable among the groups.

The maternal NOAEL is 150 mg/kg/day, and the maternal LOEL is 300 mg/kg/day, based on tremors and an increased incidence of chromodacryorrhea.

The developmental NOAEL is 300 mg/kg/day, the highest dose tested. A developmental LOAEL was not determined.

The developmental toxicity study in the rat is classified Acceptable/Guideline, and it satisfies the guideline requirement for a developmental toxicity study (OCSPP 870.3700; 83-3a) in the rodent when combined with MRID 41828001, MRID 41967201, and MRID 42520101. NOTE: The maternal NOAEL/LOAEL differ from the original assessment due to the current policy that decreases in body weight gain without significant reduction in body weight is not considered an adverse effect.

870.3700b Prenatal Developmental Toxicity Study – Rabbit

In a prenatal developmental toxicity study (MRID 00127831), New Zealand White rabbits (#/sex/dose) were administered tetrachlorvinphos (98% a.i.; T-142-3) by gavage at doses of 0, 150, 375, or 750 mg/kg/day in 5 mL/kg carboxy methylcellulose on gestation days 6-19.

Maternal toxicity at the highest dose tested was manifested as mortality (0/18, 1/18, 1/8, 2/18), abortions (0, 1, 0, 3), and red vaginal fluid (0, 1, 1, 8) in the control, low, mid, and high-dose groups, respectively.

The maternal NOEL is 375 mg/kg/day, and the maternal LOEL is 750 mg/kg/day.

Developmental toxicity at the highest dose tested was manifested as an increase in early resorptions/dam (0.4, 0.5, 0.3, 1.4), with a corresponding increase in postimplantation loss (10.6%, 5.6%, 10.5%, 21.9%) and a decrease in live fetuses/dam (7.7, 7.8, 6.9, 5.8) for the control, low, mid, and high-dose groups, respectively.

The developmental NOEL is 375 mg/kg/day, and the developmental LOEL is 750 mg/kg/day.

This developmental toxicity study in the rabbit is classified Acceptable/Guideline, and it satisfies the guideline requirement for a developmental toxicity study (OCSPP 870.3700; 83-3b) in rabbits.

A.4.3 Reproductive Toxicity

870.3800 Reproduction and Fertility Effects - Rat

In a 2-generation reproduction study (MRID 00127831), 28 Charles River CD Crl: (SD) BR Sprague Dawley rats/sex/dose were administered tetrachlorvinphos (99% a.i.; technical Rabon) *via* the diet at doses of 0, 100, 500, or 2000 ppm (F0 males: 0, 5.2, 26, or 102 mg/kg/day/F0 females: 0, 7.3, 40, or 155 mg/kg/day; F1 males: 0, 6.7, 34, or 130 mg/kg/day/F1 females: 0, 8.3, 43, or 168 mg/kg/day). Treatment of the F0 rats began when they were approximately 6 weeks old, and after 10 weeks, they were bred to produce F1 animals. Treatment continued throughout the mating, gestation, and lactation periods, with termination of the F0 rats after weaning of their litters. The F1 rats were weaned onto the same diets as their parents, and groups of 24 rats/sex/dose were selected as the F1 generation. The F1 rats were treated for 11 weeks and then mated to produce F2 litters. Treatment also continued throughout the mating, gestation, and lactation periods. Termination of the F1 and F2 animals occurred at the time of weaning of the litters.

There was no adverse effect on survival, and no clinical signs of toxicity were observed in either generation. Body weights of the adult animals were not adversely affected in either generation. Increased adrenal weights in the F0 females at 2000 ppm were considered treatment-related, although a similar increase in adrenal weight was not observed in the F1 females or in males of either generation. Fertility indices, duration of gestation, mean number of implantation sites, number of stillborns, mean litter size, pup survival, and pup body weights were comparable among the groups in both generations.

The parental NOAEL is 500 ppm (males 26/females 40 mg/kg/day). The parental LOAEL is 2000 ppm (males 102/females 155 mg/kg/day), based on increased adrenal weights of F0 females.

The offspring NOAEL is 2000 ppm (males 102/females 155 mg/kg/day). The offspring LOAEL was not identified.

The reproductive NOAEL is 2000 ppm (males 102/females 155 mg/kg/day). The reproductive LOAEL was not identified.

Note: Although minimal toxicity was observed, and higher doses would have been tolerated, cholinesterase measurements were not performed in this study. Based on findings in other studies in the TCVP database, cholinesterase inhibition would have been observed in this study, if monitored, at the mid and high dose levels.

The 2-generation reproduction toxicity study in the rat is classified Acceptable/Guideline, and it satisfies the guideline requirement for a reproduction toxicity study (OCSPP 870.3800; OECD 416) in the rodent.

A.4.4 Chronic Toxicity

870.4100a (870.4300) Chronic Toxicity – Rat

In a combined chronic toxicity/carcinogenicity study (MRID 42980901/43335101), groups of Sprague-Dawley rats (50/sex/group) were administered tetrachlorvinphos (99% a.i.) *via* the diet at dose levels of 0, 100, 1000, or 2000 ppm (males 0, 4.23, 43.2, or 88.5 mg TCVP/kg/day; females 0, 5.93, 62.7, or 125.3 mg TCVP/kg/day) for two years.

Survival was comparable among the groups in both sex, and there were no treatment-related clinical signs of toxicity. Body weight was comparable among the male groups, and females at the high dose displayed slightly lower body weights (8%-12%) than the controls from week 10 on (12% at 52 weeks; 8% at 104 weeks). Food consumption was comparable among the groups.

Females at 2000 ppm had significantly elevated cholesterol levels at weeks 77/78 and 104. Effects at 1000 and 2000 ppm in both sexes included an increased incidence and tendency to greater severity of diffuse lipidosis of the adrenal zona fasciculata, hypertrophy of periacinar hepatocytes, centriacinar degenerative (males only) changes of the liver, and reduced alkaline phosphatase activity.

RBC cholinesterase inhibition was observed in females at 1000 ppm (29%*) and 2000 ppm (36%**) at week 77/78; 18% and 22% at week 103/104 (not **). Brain cholinesterase inhibition was observed in females at 52 and 104 weeks was 17% and 16% (not **). BMDs were not run due to lack of dose-response in both compartments.

The systemic toxicity NOAEL is 100 ppm (4.23/5.93 mg/kg/day). The systemic toxicity LOAEL is 1000 ppm (43.2/62.7 mg/kg/day), based on histological liver (hypertrophy of periacinar hepatocytes in both sexes and centriacinar degenerative change in males) and adrenal changes (increased incidence of diffuse lipidosis of adrenal zona fasciculata in both sexes).

Increased incidence of thyroid C-cell adenomas was observed in male rats at the highest dose and adrenal pheochromocytomas were observed in males.(both sexes). The LEL is 1000 ppm, based on decreased body weight in females, histological liver and adrenal changes in both sexes.

The study is classified Acceptable/Guideline, and it satisfies the guideline requirements for a combined chronic toxicity/carcinogenicity study (OCSPP 870.4300; OECD 453), a chronic oral toxicity study (870.4100; OECD 452), and a carcinogenicity study (870.4200; OECD 451) in the rodent.

870.4100b Chronic Toxicity – Dog

In a chronic oral toxicity study (MRID 42679401), tetrachlorvinphos (TCVP; 99% a.i.; Batch 01-KMJ-012) was given to outbred Beagle dogs (4/sex/group) *via* capsule at doses of 0, 6.25, 500, or 1000 mg/kg/day for 52 weeks.

Survival was not adversely affected in either sex, and there were no clinical signs of toxicity. There were no treatment-related effects on body weight or food or water consumption, and no differences in ophthalmologic, macroscopic, and microscopic findings in either sex.

Treatment-related decreases in red blood cell counts at 500 and 1000 mg/kg/day were corroborated by decreases in hemoglobin, mean corpuscular hemoglobin concentration, and hematocrit, and increases in mean corpuscular volume. The kidney and liver weight increases at 500 and 1000 mg/kg/day in both sexes may be related to the alkaline phosphatase increases (both sexes) and cholesterol decreases (males) observed, but no histopathological correlates were evident. The decreases in urine specific gravity at 500 and 1000 mg/kg/day in both sexes may be related to the kidney weight increases at these dose levels, but histopathological correlates were not evident.

RBC and brain cholinesterase inhibition were not observed at any dose level in either sex at any time point monitored.

The systemic toxicity NOAEL is 6.25 mg/kg/day. The systemic toxicity LOAEL is 500 mg/kg/day, based on decreased red blood cell counts, hemoglobin, hematocrit, MCHC, MCV, alkaline phosphatase, urine specific gravity, and decreased liver and kidney weights.

The chronic toxicity study is classified Acceptable/Guideline, and it satisfies the guideline requirement for a chronic toxicity study (OCSPP 870.4100; OECD 452) in the non-rodent.

A.4.5 Carcinogenicity

870.4200a Carcinogenicity Study – Rat

In the combined chronic toxicity study (MRID 42980901/43335101), groups of 50 male and 50 female Charles River Sprague-Dawley rats received TCVP in their diet over a 2-year period at 0, 100, 1000 or 2000 ppm (equivalent to 0, 4, 43 and 89 mg/kg/day in males and 0, 6, 63 and 125 mg/kg/day in females, respectively). See above under 870.4100a.

There were increases in the incidences of thyroid C-cell adenomas and adrenal pheochromocytomas in male rats only. Neither of these increases were statistically significant by pairwise comparison to controls, but there was a statistically significant increasing trend for the adrenal tumors.

This study is classified as Acceptable/Guideline, and it satisfies the guideline requirements (870.4200; OECD 451] for a carcinogenicity study in the rat.

In another rat study (MRID 00117443; 1978 NCI-sponsored Gulf South study), Osborne-Mendel rats received TCVP in their diet at doses of 0, 4250, or 8500 ppm for 80 weeks, followed by 31 weeks observation.

Statistically significant increase in the incidences of adrenal cortical adenomas and thyroid C-cell adenomas were found in dosed female rats. High incidences of thyroid C-cell hyperplasia in both sexes further indicated an effect on the thyroid.

This study is classified Acceptable/Non-Guideline, and it does not satisfy the guideline requirement (870.4200; OECD 451) for a carcinogenicity study.

870.4200b Carcinogenicity – Mouse

In a carcinogenicity study (MRID 00126039), B6C3F1 mice were fed diets containing 0, 17.5, 64, 320, 1600, 8000, or 16000 ppm tetrachlorvinphos for two years in a carcinogenicity study. For systemic toxicity, the NOAEL was 1600 ppm (240 mg/kg/day) and the LOAEL was 8000 ppm (1200 mg/kg/day), based on decreased weight gain. Administration of TCVP in the diet to B6C3F1 mice resulted in statistically significant increases in hepatocellular adenomas, carcinomas and combined adenomas/carcinomas (with carcinomas predominant) in females, and in combined hepatocellular adenomas/carcinomas in males. In male mice there were also statistically significant increases in renal adenomas, carcinomas and combined adenomas/ carcinomas. The statistically significant increases in tumors noted above, all occurred only at doses of TCVP of 8000 ppm or greater, except for the combined hepatocellular adenomas/ carcinomas in female mice, which also occurred at 1600 ppm.

This study is classified as Acceptable/guideline, and it satisfies the guideline requirements (870.4200; OECD 451] for a carcinogenicity study in the mouse.

In another carcinogenicity study (MRID 00117443), B6C3F1 mice were fed diets containing 0, 8000, or 16000 ppm TCVP for 80 weeks, followed by 12 weeks observation. Increased incidences of hepatocellular carcinomas and granulomatous lesions of the liver were found in the dosed mice.

This study is classified Acceptable/Non-Guideline, and it does not satisfy the guideline requirement (870.4200; OECD 451) for a carcinogenicity study in the mouse.

A.4.6 Mutagenicity

Summary of the Genotoxicity Studies for TCVP			
Guideline No.	**Study Type**	**MRID No. (year)/ Classification /Doses**	**Results**
GENE MUTATION			
870.5100	Bacterial Reverse Gene Mutation Assay in *Salmonella typhimurium*	4122508 (1989) Acceptable/guideline 0, 10-667 µg/plate -S9 0, 66.7-3300 µg/plate +S9	**Negative** up to cytotoxic concentrations at the highest dose tested +/-S9
CHROMOSOME ABERRATIONS			
870.5375	*In vitro* Mammalian Cell Clastogenicity Assay in Chinese hamster ovary (CHO) cells	41312901 (1989) Acceptable/guideline 0, 29.9, 44.9, 59.9, 79.8, 99.8 µg/mL -S9 (20-hr cell harvest) 0, 12.5, 25, 37.6, 75.1 µg/mL, +S9 (10-hr cell harvest)	**Positive** Significant & dose-related increases in chromosome aberrations in the absence of S9 only after a prolonged exposure due to severe mitotic delay, unhealthy monolayers and reduced mitotic cells at 59.9 & 79.8 µg/mL. Major aberrations: chromatid & chromosome breaks NOTE: Increases in chromosome aberrations were accompanied by marked increases in chromatid & chromosome gaps. **Negative** with S9 activation up to a precipitating (≥676 µg/mL) & cytotoxic (2030 µg/mL) concentrations
	In vitro Mammalian Cell Clastogenicity Assay in Mouse spleen cells	Amer & Aly (1992) Acceptable/nonguideline 0.25, 0.5, 1.0, 2.0 µg/mL (4-hr treatment)	**Chromosome aberrations** **Positive:** Significant & dose-related increases in chromosome aberrations (minus gaps) at ≥0.5 µg/mL Major aberrations: chromatid & chromosome fragments NOTE: Increases in chromosome aberrations were accompanied by marked increases in chromatid & chromosome gaps. **Sister Chromatid Exchange (SCE)** **Positive:** Significant & dose-related increases in SCE induction at ≥0.5 µg/mL

Summary of the Genotoxicity Studies for TCVP			
Guideline No.	**Study Type**	**MRID No. (year)/ Classification /Doses**	**Results**
	Micronucleus Assay in Bone Marrow Cells of the Mouse	Amer & Aly (1992) **Oral:** 0, 3000 & 6000 ppm dietary administration daily for 14 consecutive days or 10 weeks **Ip injection**: 0, 50 & 100 mg/kg weekly for 2 weeks **Dermal:** 0, 1350 mg/kg 4 treatments	**ORAL:** S↑ % PCEs at 3000 & 6000 ppm after 10 weeks at 24 hours & 7 & 14 days post-treatment but **S↑% MPCEs only 6000-ppm group at 24 hours & 7 days post-treatment** **IP INJECTION**: **<u>50 mg/kg</u>: S↑ % MPCEs at 24 hr. post-treatment (Double injection only); % PCEs not reported.** **<u>100 mg/kg</u> (single injection): S↑ % PCEs at 24 hr. post-treatment only.** **<u>100 mg/kg</u> (double injection): S↑ % PCEs at 24 hr. post-treatment** **S↑ % MPCEs at 24 hr. post-treatment only.** **DERMAL:** S↑ % PCEs at 24 hr. post-treatment 1350 mg/kg (4 applications) only; no increase in MPCEs
OTHER MUTAGENIC MECHANISMS			
870.5550	*In vitro* unscheduled DNA synthesis (UDS) in primary rat hepatocytes	42156401 (1992) Acceptable/guideline 0, 10-40 µg/mL (9 doses)	**Negative** Cytotoxicity was observed as follows: 35 & 40 µg/mL -lethal 23-30 µg/mL (moderate to high cytotoxicity) 15 & 20 µg/mL (slight cytotoxicity) 10 µg/mL (non-cytotoxic)
	DNA adduct formation Swiss male mice liver.	Zayed et al., 1983) 25, 50 and 100 mg/kg i.p. injection	**Positive** Fraction of total applied dose associated with 7-methyl guanine was estimated to be $9x10^{-5}$ and $39x10^{-5}$ in DNA and RNA, respectively.

The relevance of the mutagenic findings to the tumorigenic response seen in female mice cannot be established. Therefore, a follow-up mouse micronucleus assay (OPPTS Harmonized Guideline 870.5395) is required for TCVP. Additionally, a study that investigates possible genotoxic activity in the target organ (liver) is required. This study should examine DNA damage potential (Comet assay, DNA adduct formation, or any other DNA target)[41].

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[41] N. McCarroll and D. Davis, 12/21/2016, Tetrachlorovinphos (TCVP): Revisit of Mutagenicity Studies, TXR#0057553, D437226.

A.4.7 Neurotoxicity

870.6100b Delayed Neurotoxicity – Hen

In an acute delayed neurotoxicity study in hens (MRID 41905901), technical Rabon (tetrachlorvinphos; Lot # 01-KMJ-012; 99% a.i.), was administered twice orally (Mazola corn oil) to hens at 2500 mg/kg, with an intervening 21-day period (total dose 5000 mg/kg).

There was sufficient evidence of acute toxicity, including mortality (4/15), to establish that the test material was administered at a sufficiently high dose. TCVP did not result in delayed neurotoxicity, as evidenced both by in-life observations and microscopic examination of spinal cord tissue from three levels. The minimum myelin degeneration seen in 2 hens was consistent with the normal background incidence for this finding in this type of study. The positive control material (tri-0-tolyl- phosphate, TOTP) at 1000 mg/kg elicited the appropriate response.

This study is classified **as Acceptable/Guideline** and it satisfies the guideline requirement for a delayed neurotoxicity study in the hen (870.6100).

870.6200a Acute Neurotoxicity Screening Battery – Rat

In an acute neurotoxicity study (MRID 42912501), tetrachlorvinphos (99% a.i.; Lot #: 01-KMJ-012) was administered *via* gavage (10 mL/kg; in corn oil) to non-fasted Sprague-Dawley Crl:CD®BR rats (12/sex/dose) at doses of 0, 65, 325, or 650 mg/kg. All rats were evaluated in functional observational batteries and motor function observations on days 0, 7, and 14.

Transient neurotoxic effects were observed in both sexes on day 0 at the mid- and high-dose levels. These effects were consistent with cholinesterase inhibition. At 650 mg/kg, the predominant clinical signs observed in both sexes on the day following dosing consisted of gait alterations (prostration, rocking, lurching, and swaying when ambulatory; walked on tiptoes), constricted pupils, tremors (fore- and hindlimb), cool body to the touch, yellow material on various body surfaces, red material on forelimbs, around eyes, nose, and mouth, and/or increased defecation. Several of these findings were noted in a limited number of rats (mainly females) on days 2, 3, 4, and/or 5. At 325 mg/kg, one female showed gait alterations and one male and 3 females had constricted pupils on day 1. The neuropathologic examination gave no indication of any dose-related permanent effects on the brain or in the peripheral or central nervous tissues, consistent with the lack of permanent changes in muscular coordination and/or behavior.

The NOAEL is 65 mg/kg, and the LOAEL is 325 mg/kg, based on transient neurotoxic effects in both sexes on day 0.

This study is classified **as Acceptable/Guideline,** and it satisfies the guideline requirement for an acute neurotoxicity study in rats (OPPTS 870.6200, OECD 424).

870.6200b Subchronic Neurotoxicity Screening Battery - Rat

In a subchronic neurotoxicity study (MRID 43294101), tetrachlorvinphos (99% a.i.; Lot #01-KMJ-012) was administered via the diet to 10 Sprague-Dawley Crl:CD®BR rats for 90 days at dose levels of 0, 200, 1000, or 5000 ppm. A Functional Operational battery (FOB) and motor activity were assessed at weeks -1, 0, 3, 7, and 12.

There were no deaths or clinical signs of toxicity. There were no measurement of cholinesterase activity, but cholinergic signs were not observed. Decreased body weight was observed throughout the study in males at 5000 ppm (8%-9%) and in females at 2000 ppm (8%-10%) and 5000 ppm (7%-13%). There were no indications of any dose-related effects during the home-cage, handling, open-field, sensory or neuromuscular observations. There were no significant dose-related differences between groups involving group mean motor activity counts. Brain weights and brain measurements (weight and morphometric) were comparable among the groups for both sexes, and there were no differences in histomorphological neurology findings between the control and 5000 ppm groups.

The NOAEL is 5000 ppm (250 mg/kg/day; standard conversion). The LOAEL was not identified.

This study is classified **as Acceptable/Guideline,** and it satisfies the guideline requirement for a subchronic neurotoxicity study in rats (OPPTS 870.6200, OECD 424).

870.6300 Developmental Neurotoxicity - Rat

In a developmental neurotoxicity study (MRID 46660601), tetrachlorvinphos (99.6% a.i.; Lot #: NJ250RB08) in aqueous 1% (w/v) methylcellulose was administered via gavage (10 mL/kg) to pregnant Sprague-Dawley rats (25/dose) from gestation day (GD) 6 to lactation day (LD) 6 at doses of 0, 10, 50, or 200 mg/kg/day. Additionally, the F_1 pups were similarly dosed on postnatal days (PNDs) 7-21. Dams were allowed to deliver naturally and were sacrificed on LD 21. On PND 4, litters were standardized to 10 pups/litter; the remaining offspring and dams were sacrificed and subjected to a gross necropsy. Subsequently, 1 pup/sex/litter/group (at least 10 pups/sex/dose when available) were allocated to the following subsets: Subset 1, PND 21 brain weights and neurohistological evaluations; Subset 2, water maze and passive avoidance test; Subset 3, motor activity and auditory startle habituation; Subset 4, terminal brain weights and neurohistological evaluations; and Subset 5, standardize litter size to ten pups (5 male and 5 female) per litter on PND 4-21.

In dams, there were no treatment-related effects on mortality, clinical signs, body weight, body weight gain, feed consumption, FOB, or gross pathology. No treatment-related effects on reproductive parameters were observed. **The maternal LOAEL was not observed. The maternal NOAEL was 200 mg/kg/day (HDT).**

In offspring, there were no treatment-related effects on viability, litter observations, clinical signs, body weight, food consumption, FOB, motor activity, acoustic startle habituation, learning and memory (passive avoidance and water maze), gross pathology, or histopathology parameters.

At 200 mg/kg/day, decreases ($p \leq 0.05$) in body weight were noted in the males (↓5-8%) on PNDs 15 and 16 (pre-weaning) and PND 22 (post-weaning) and in the females (↓6%) on PND 29 (post-weaning). Body weight gains were decreased ($p \leq 0.05$) during pre-weaning at several intervals in the males (↓12-28%) and females (↓13-26%). Decreases ($p \leq 0.05$) in body weight gains during post-weaning were observed in the males on PNDs 21-22 (↓36%) and in the females on PNDs 21-22 and 22-29 (↓7-28%). Absolute brain weight was decreased ($p \leq 0.01$) by 8% in the males. This finding was judged to correlate with the treatment-related decreases ($p \leq 0.05$) in several microscopic linear brain measurements: (i) thickness of the striatum on PND 21 (↓4-5% both sexes) and PND 70 (↓7% males only); (ii) thickness of the corpus callosum on PND 70 (↓16-21% both sexes); (iii) thickness of the hippocampal gyrus on PND 70 (↓7-9% both sexes); and (iv) height of the cerebellum on PND 70 (↓7% males only). It is noted that on PND 21, decrease in single morphometric parameter was seen in both sexes with the small magnitude (4-5%) whereas on PND 70, decrease in multiple morphometric measurements were seen in both sexes with greater magnitude (7-21%) than that seen in PND 21.

No treatment related effects were noted in the ≤50 mg/kg/day F_1 offspring.

The offspring LOAEL was 200 mg/kg/day, based on decreases in body weight, body weight gains and several morphometric linear brain measurements in both sexes, and decreased absolute brain weight in the males on PND 70. The offspring NOAEL was 50 mg/kg/day.

This study is classified **as Acceptable/Guideline,** and it satisfies the guideline requirement for a developmental neurotoxicity study in rats (OPPTS 870.6300, §83-6; OECD 426) in the rat.

A.4.8 Metabolism

870.7485 Metabolism – Rat

In a metabolism study (MRID 41988401), single oral doses of ^{14}C-tetrachlorvinphos (97%; Lot # 2587-180; ^{14}C in the phenyl group) were administered *via* gavage to three groups of Sprague-Dawley rats (5/sex) at (A) 5 mg/kg, (B) 5 mg/kg following 14 consecutive doses of unlabeled test material, or (C) 250 mg/kg, and urine (0-8 hours, 8-24 hours, and at 24-hour intervals up to 120 hours post dose) and feces (at 24-hour intervals up to 120 hours post dose) were collected. At 120 hours post dose, the rats were sacrificed, and whole blood/plasma, heart, lungs, liver, kidney, spleen, gastrointestinal tract, brain, ovaries/testes, total skin, and samples of muscle, fat, and bone, and the remaining carcass were collected for analysis.

Most of the radioactivity was recovered in urine (46%-60%) and feces (38%-56%) within 48 hours post dose. The greatest activity in the urine was found in the 0-8 hour interval for both sexes following the single and repeat 5 mg/kg dose, whereas the greatest activity following the 250 mg/kg dose was found in the 8-24 hour interval. Following the single 250 mg/kg dose, males excreted a similar % (≈50%) of the dose *via* the urine and feces, whereas the females excreted the majority *via* the urine (70% vs 30%). Following the single 5 mg/kg dose, males excreted 60%

via the urine and 40% via the feces, and females excreted equal amounts (≈50%) *via* the urine and feces. Following the 14-day dosing period, both sexes excreted approximately equal amounts (≈50%) *via* the urine and feces. Only minor amounts (<0.5%) of the radiolabel were recovered from tissues after 5 days, with the GI tract, whole blood, and lungs showing the highest concentrations. The major metabolite in urine was trichloromandelic acid (18%-26%), and the major metabolite in feces was trichlorophenylethanol (>13%). Since the oral LD50 for female rats is lower than the male LD50, it is noteworthy that males of all groups excreted more total label as trichloromandelic acid, a more completely metabolized form of TCVP, whereas the high-dose females tended to excrete more of the label as desmethyl TCVP (with the phosphate group still attached to the remainder of the molecule), a compound that could be derived from TCVP with only a single metabolic step.

The metabolism study is classified as Acceptable/Guideline, and it satisfies the guideline requirement for a metabolism study (OPPTS 870.7485, OECD 417) in rodents.

870.7600 Dermal Penetration Study – Rat

In a dermal absorption study (MRID 42111501), male CD rats (28/group/time point) were exposed dermally to doses of 0.01, 0.1, 1 or 5 mg/cm^2 radiolableled tetrachlorvinphos (97% a.i.), with some of each dose group sacrificed at 0.5, 1, 2, 4, or 10 hours. Additionally, there was a group of animals, sacrificed at 72 hours, in which the skin was washed at 10 hours. The area of the dermal application was washed to recover unabsorbed tetrachlorvinphos. Then, the skin, urine, feces, and carcass were analyzed for percent of total tetrachlorvinphos applied. For the group sacrificed at 10 hours, 84 % of the total tetrachlorvinphos applied (0.1 mg/cm^2) was recovered in the wash, and 9.57 % was in the skin, urine, feces, and carcass. The percent absorption increased with duration of exposure and generally decreased with increasing dose. The actual quantity of tetrachlorvinphos absorbed increased with increasing dose.

This study is classified as **Acceptable/Guideline**, and it satisfies the guideline requirement (OCSPP 870.7600) for a dermal penetration study in the rat.

A.4.9 Immunotoxicity

870.7800

In an immunotoxicity study (MRID # 48794701), Tetrachlorvinphos [100.05%, lot #100113] was administered to Crl:CD-1(ICR) female mice (10/dose) via oral gavage at dose levels of 0, 75, 300, or 1200 mg/kg/day for 28 consecutive days. An additional group of 10 positive control females received cyclophosphamide 10 mg/kg/day via gavage for 28 days. On Day 25 a single intravenous (IV) dose of 0.25 mL/animal of sheep red blood cells (SRBC) 2x10^8 cells/animal was administered to all animals. During the study, clinical signs, morbidity and mortality, bodyweight, food consumption, water consumption were measured and evaluated. On Day 29, blood samples were collected from the orbital sinus under isoflurance anaesthesia. Animals were euthanized

with carbon dioxide followed by exsanguination. All animals were subject to a complete necropsy examination. Spleen and thymus weights were recorded and immunotoxicity investigations by an Enzyme-linked immunosorbent assay (ELISA).

There were no treatment-related clinical signs and no unscheduled deaths. There were no treatment-related effects on body weights, food or water consumption. There were no treatment related necropsy findings. Absolute and relative mean thymus weight were statistically significantly lower ($p<0.05$) at 300 mg/kg/day group when compared with the vehicle control group. There were lower mean absolute thymus weight at 1200 mg/kg/day but it was not statistically significant; and there was no dose-dependent response in treated groups. Spleen weights in treated groups were not significantly different from the vehicle control group.

For systemic toxicity, the NOAEL is 1200 mg/kg/day, the LOAEL was not established.

When compare to the vehicle control group, the low and mid dose groups (75 and 300 mg/kg/day) had slightly higher anti-SRBC IgM levels, and the highest dose group (1200 mg/kg/day) had lower IgM levels. However, there were no statistically significant treatment-related effects on the specific anti-SRBC antibody response. High inter-individual variability was noted in all the treatment groups as well as in the control group. Evaluation of the individual animal data of this study did not show any trend or distribution that would demonstrate significant suppression of anti-SRBC IgM response. Animals in positive control group showed a statistically significant ($p< 0.05$) decrease of the anti-SRBC IgM response. This confirmed the ability of the test system to detect immuno-suppressive effects and confirmed the validity of the study design.

The NK cells activity assay was not performed. The toxicology database for tetrachlorvinphos does not reveal any evidence of treatment-related effects on the immune system. The overall weight of evidence suggests that this chemical does not directly target the immune system. Under HED guidance, a NK cells activity assay is not required at this time.

For immunotoxicity, the NOAEL is 1200 mg/kg/day, tested above the limit dose; the LOAEL was not established.

This immunotoxicity study is classified **acceptable/ guideline**, and satisfies the guideline requirement for an immunotoxicity study (OPPTS 870.7800) in mice.

Special Studies

Comparative Cholinesterase Studies

A series of studies (acute, repeat, gestational) was performed to investigate the effect of TCVP on brain and blood cholinesterase (ChE) activity and to determine the peak time of ChE

inhibition following both acute and repeated dosing in pre-weaning, young, maternal, and adult Sprague Dawley rats.

Comparative Cholinesterase Assay - Repeat (11-days) Dose:

In a comparative cholinesterase study (2012, MRID No.: 48773401), five groups of 10/sex of both 11 day old and young adult (~61 days) Crl:CD(SD) strain rats were dosed *via* gavage at dose levels of 0, 5, 10, 50 or 200 mg/kg/day of tetrachlorvinphos (TCVP) in methylcellulose. After 11 doses, the rats were sacrificed and assessed for red blood cell (RBC) and brain cholinesterase (ChE) activity.

Systemic effects. One female pup in the high dose group died after only two doses and its death was attributed to treatment. There was some decrease in body weight in this rat pup prior to death and the appearance was described as moderately dehydrated but no signs of typical ChE inhibition toxicity were reported. No other pups demonstrated clinical signs. There was an initial negative body weight gain in the adult males (days 1-2) but no clinical signs were evident in the adults.

The LOAEL for systemic effects for both ages is 200 mg/kg/day, based on a single death of a female pup. The NOAEL is 50 mg/kg/day.

RBC ChE inhibition. Adult males demonstrated a statistically significant reduction (13.3%) in RBC ChE level at 10 mg/kg/day. At 50 mg/kg/day, both male pups and adults had similar levels of inhibition (30% to 33%). At 200 mg/kg/day, the male pups were inhibited more (59.9%) than the male adults (36.3%). At 50 mg/kg/day, adult females demonstrated more inhibition (40.6%) than the female pups (19.2%) but at 200 mg/kg/day both female pups and adults had ~62% inhibition.

The LOAEL for RBC ChE inhibition is 50 mg/kg/day for both sexes and both ages. The NOAEL is 10 mg/kg/day.

Brain ChE. There was a dose-related decrease in brain ChE in adult females that was statistically significant at 10 mg/kg/day (↓12.2%), 50 mg/kg/day (↓42%), and 200 mg/kg/day (↓57.2%). Both sexes of pups displayed similar levels of brain ChE inhibition at 50 mg/kg/day (males ↓15.7%/females ↓18.7%) and 200 mg/kg/day (males ↓46.3%/females ↓45.1%), which were statistically significant. The adult males displayed statistically significant brain ChE inhibition at 50 mg/kg/day (↓14.9%) and 200 mg/kg/day (↓17.8%), although the magnitude of the response was similar at both dose levels.

The LOAEL for brain ChE inhibition is 10 mg/kg/day, based on significant inhibition in adult females. The NOAEL is 5 mg/kg/day in adult females. The LOAEL for brain ChE inhibition is 50 mg/kg/day in male and female pups and in male adults. The NOAEL in male and female pups and in male adults is 10 mg/kg/day.

Overall conclusion. The main objective of this study was to determine if the pups are more sensitive than the adults to the cholinesterase inhibitory potential of TCVP. A comparison of the magnitude of cholinesterase inhibition in the brain and RBC compartments in the females shows the female pups with less inhibition (at 50 mg/kg/day) or a comparable amount of inhibition (at 200 mg/kg/day) as the female adults. For the males, a similar magnitude of inhibition was displayed in the pups and adults at 50 mg/kg/day, although the male pups displayed a greater % inhibition in both compartments at 200 mg/kg/day than the adult males. Based on assignment of the NOAEL and LOAEL, there was no demonstration for increased sensitivity of the pups relative to the adults for either RBC or brain ChE. Although the magnitude of brain inhibition in the male pups was greater than in the male adults, this occurred only at the 200 mg/kg/day dose level. The benchmark dose analysis of the brain cholinesterase data does not show the male pups to be more sensitive.

A benchmark dose analysis of the repeat dose cholinesterase data (RBC and brain) was performed that provides both the BMD_{10} and $BMDL_{10}$ of adults and PND11 pups.

BMD_{10}s and $BMDL_{10}$s for Adult Rat and PND 11 Pup Cholinesterase				
	RBC BMD_{10}	**RBC $BMDL_{10}$**	**Brain BMD_{10}**	**Brain $BMDL_{10}$**
Adult males	7.7178	3.5942	33.803	24.4489
Adult females	8.6762	6.1335	7.1764	5.4980
PND 11 males	20.4688	15.9719	33.4825	26.5707
PND 11 females	20.5608	13.1692	24.2224	18.9412

Classification: The classification of this repeat dose *in vivo* comparative cholinesterase inhibition study is Acceptable/Non-Guideline. It does not satisfy a guideline requirement. It satisfies the generic data call-in requirement for TCVP for a comparative cholinesterase study in adult rats versus postnatal day (PND) 11 rat pups.

Comparative Cholinesterase Assay - Acute Dose

In an acute comparative cholinesterase study (MRID 48773401a), TCVP (98.99% a.i.; Batch # TX100405)] was administered to 10 Crl:CD (SD) adult rats/sex/dose, 10 Crl:CD (SD) postnatal day (PND) 11 pups/sex/dose, and 10 Crl:CD(SD) PND 21 pups/sex/dose once *via* gavage (10 mL/kg) at dose levels of 0 (1% w/v aqueous methylcellulose), 10, 50, 150, or 300 mg/kg. Viability, clinical signs, body weights, and brain weights were evaluated. Approximately three hours post dose, red blood cell (RBC) and brain acetylcholinesterase (AChE) levels were determined.

There were no treatment-related deaths. Treatment-related clinical signs included soft or liquid feces in several adult males at 150 mg/kg and 300 mg/kg, decreased motor activity in PND 21 males and females at 150 mg/kg and 300 mg/kg, and urine-stained abdominal fur in PND 21 rats at 300 mg/kg. There were no clinical signs in the PND 11 pups or adult females.

Cholinesterase inhibition was displayed in both compartments in all age groups at all dose levels, with one exception. The magnitude of the response in the adult female rats (RBC and brain) was lower than in the adult male rats and in both sexes of PND 11 and PND 21 pups.

For both compartments, the magnitude of the response was comparable among the age groups and similar between the sexes, with the exception of the adult female rats. *All groups showed a similar response in both the RBC and brain cholinesterase compartments at each dose level.*

The NOAEL for adult rats (both sexes) for RBC and brain cholinesterase inhibition following an acute oral dose was not determined. The LOAEL for adult rats is 10 mg/kg.

The NOAEL for PND 21 pups could not be determined, based on RBC and brain cholinesterase inhibition at all dose levels following acute oral exposure. The LOAEL for PND 21 pups is 10 mg/kg.

The NOAEL for PND 11 pups could not be determined, based on RBC and brain cholinesterase inhibition at all dose levels following acute oral exposure. The LOAEL for PND 11 pups is 10 mg/kg.

This comparative study of RBC and brain cholinesterase activities following acute oral treatment with TCVP in adult and neonatal (PND 11 and PND 21) rats is classified **Acceptable/Non-guideline.** It does not satisfy any guideline requirement; however, it does satisfy the data requirement for TCVP for an acute comparative cholinesterase activity between adult and young rats.

COMMENT: This acute exposure comparative cholinesterase study final report was embedded within the repeat dose comparative cholinesterase study report (MRID 48773401); it should have been submitted as a separate study report and been given a unique MRID #. The results of the Benchmark dose analysis for the acute study are provided below.

TCVP/Study	Sex/Age	Compartment	BMD Results (mg/kg)	
			BMD_{10}	$BMDL_{10}$
MRID 48773401a Acute CCA	Male PND11	Brain	5.1	4.5
	Female PND11	Brain	5.9	4.8
MRID 48773401a Acute CCA	Male PND11	RBC	5.0	4.1
	Female PND11	RBC	3.4	2.8
MRID 48773401a Acute CCA	Male PND21	Brain	3.5	3.2
	Female PND21	Brain	5.3	3.7
MRID 48773401a Acute CCA	Male PND21	RBC	3.2	2.8
	Female PND21	RBC	4.6	2.8
MRID 48773401a Acute CCA	Male Adult	Brain	7.4	5.6
	Female Adult	Brain	11.6	9.8
MRID 48773401a	Male Adult	RBC	6.5	3.6

Acute CCA	Female Adult	RBC	14.9	11.2

Comparative Cholinesterase Assay - Gestational Exposure

In a maternal and fetal exposure study (2010, MRID 48291101), tetrachlorvinphos (TCVP) (purity 99.6%, Lot No. NJ250RB08) dissolved in 1% aqueous (w/v) methylcellulose was administered to pregnant female Crl:CD(SD)IGS BR VAF/Plus rats via gavage once daily on days 6 through 21 of gestation at doses of 0, 75, 150 or 300 mg/kg/day. On gestation day 21 (GD 21), within 2 hr of the last dose, whole blood samples and brains were collected from the dams for cholinesterase (ChE) assessment. Dams were Caesarean-sectioned and pooled fetal blood samples and brains were collected for ChE assessment.

Maternal Systemic and Litter Effects: All dams survived until scheduled sacrifice and no adverse clinical observations were reported. No Caesarean-sectioning or litter parameters were affected. Body weight *gains* and food consumption in dams were reduced in the 150 and 300 mg/kg/day groups. No gross lesions were observed during necropsy of the dams. There were no fetal gross external alterations and fetal body weights, brain absolute and relative weights were comparable among the dose groups. Since the main purpose of this study was to assess differential sensitivity between the dams and the fetuses, no assignment of a NOAEL and LOAEL for maternal systemic and litter effects is being made.

RBC ChE: Neither the dams nor the fetuses demonstrated RBC ChE inhibition. In dams the values were 5.1%, 15% and 3% lower than the control for the low, mid and high doses, respectively. Interpretation of the fetal RBC data was confounded because only 1 or two samples were available and no sample was available for the mid dose group. *The RBC ChE data are considered unacceptable because the repeat dosing study (2012, 48773401) conducted in the same laboratory in the same strain of rat was clearly able to demonstrate RBC ChE inhibition at 50 and 200 mg/kg/day in females. There was no way to compare adult and fetal RBC ChE.*

Plasma ChE. Plasma ChE inhibition in dams was dose dependent being 62%, 71% and 77% for the low, mid and high dose groups, respectively. Fetal plasma ChE values were 22%, 18.5% and 20.8% less than the control for the low, mid and high dose groups, respectively. The lack of a dose response raises the question as to whether these lower values are actually inhibition. However, there is no indication that the fetuses are more sensitive than the dams for this compartment.

Brain ChE. Brain ChE inhibition was also dose dependent in dams; *i.e.*, 31%, 44% and 67% for the low, mid and high doses, respectively. Fetal brain ChE values were 10%, 20.9% and 20.8% lower than the controls for the low, mid and high dose groups, respectively. Similar to the plasma ChE data, there is no dose response to support a conclusion that these lower values are actually inhibition. However, there is no indication that the fetal brain ChE is more sensitive to inhibition by TCVP than the dams.

This *in vivo* comparative ChE study is classified as **Acceptable/non-guideline**. The study does not satisfy a guideline requirement. It satisfies a data call-in-requirement for TCVP for a gestational comparative ChE study in maternal rats versus fetal rats, although it is to be noted that the dose levels selected are way too high. However, from the data available, no increase in sensitivity was evident. RBC ChE inhibition was not demonstrated in the dams or fetuses (no data), and the flat dose response curves for the brain ChE in both pups and adults confound the interpretation of the study. However, no additional gestational CCA study is being requested at this time because there is no indication that the fetuses were more affected than the dams.

Comparative Cholinesterase Assay - Acute Exposure

In an acute relative cholinesterase (ChE) sensitivity study (2010, MRID 48294601), tetrachlorvinphos (TCVP) (purity 99.6%, Lot No. NJ250RB08) was administered at doses of 0, 75, 150 or 300 mg/kg body weight dissolved in 1% aqueous (w/v) methylcellulose to Crl:CD(SD)IGS BR VAF/Plus strain young adult (about 42 days old) and to postnatal day (PND) 11 and 21 neonatal rats via a single oral (gavage) dose. Four rats/sex/dose were sacrificed on pretest and at 1, 2, 3, 4, 8 and 24 hours after dosing.

Systemic effects. All pups and all adult rats groups survived. There were no adverse clinical or necropsy observations related to the TCVP administration, and no effects on body or brain weights were reported. Since this is a short term study primarily designed to assess for comparative sensitivity to ChE inhibition, no NOAEL or LOAEL for systemic effects will be assigned.

General comments on ChE assessment. Only four rats/sex were available for assessment at each of the seven assessment times. Many of the RBC and plasma ChE assessments were made on only 0 (no sample available), 1, 2, or 3 samples because of loss of sample. In addition, duplicate samples that did not replicate contributed to the low number of sample to provide a meaningful mean. Brain ChE also appeared to be affected by the low number of samples. The results for all three enzyme sources indicated that there was inhibition at all doses but there was poor dose response with the degree of apparent inhibition at the higher doses often less that at the low dose of 75 mg/kg/day. There was also a lack of temporal concordance with high apparent inhibition at one time, a much lower degree at the following time and back to the higher level at the next time point. Another problem is that there was more or similar apparent inhibition at the low dose of 75mg/kg in this acute study than there was in the repeat dosing studies (2012, MRID 48773401, eleven daily doses) at 200 mg/kg/day and in the gestational study (2010, MRID 48291101, fifteen daily doses) at 150 mg/kg/day. Also, the repeat dosing study clearly indicated that there was no increase in sensitivity of the pups relative to the adults with regard to potential inhibition by TCVP. In this acute study, there were several comparisons among the PND11, PND21 and adults that suggested the pups were more sensitive.

Overall, there is little confidence in the data mainly because of the lack of clear dose and temporal responses.

Benchmark Dose (BMD) modeling. BMD modeling was performed but could not be done with the RBC data or for the PND11 brain data because of too few samples and/or the data would not otherwise fit the models. BMD modeling for the brain data (for the three hour assessment time) indicated that for males, the adults may be slightly more sensitive than the PND 21 pups but the females were considered similar with respect to the BMD_{10} and $BMDL_{10}$.

TCVP/Study	**Sex/Age**	**Compartment**	**BMD Results** (mg/kg/day)	
			BMD_{10}	**$BMDL_{10}$**
MRID 48294601 Acute CCA	Adult male	Brain	6.76716	5.02249
MRID 48294601 Acute CCA	Adult female	Brain	11.2932	4.55107
MRID 48294601 Acute CCA	Male pup PND 21	RBC	16.8647	9.71265
MRID 48294601 Acute CCA	Female pup PND 21	Brain	9.80073	4.6942
MRID 48294601 Acute CCA	Male pup PND 21	Brain	11.246	6.76389

This study is classified as **Acceptable/Non-Guideline.** The study does not satisfy a guideline requirement. It satisfies a data call-in-requirement for TCVP for an acute comparative ChE study in adult, PND 21, and PND 11 pups, although there is too much variability in the data to make meaningful comparisons for sensitivity for RBC. Brain ChE data also had problems with variability and dose response to compare for sensitivity. However, from the data available, there is no conclusive evidence of increased sensitivity. No additional acute CCA study is being requested at this time because there is no indication that the young animal was more affected than the adult. NOTE: An additional acute comparative cholinesterase study (MRID 48773401a) was located and is discussed above.

Appendix B. Results for BMD/BMDL modeling for TCVP

B.1. Summary of OPP's ChE Policy & Use of BMD Modeling

OPP's AChE policy (USEPA, 2000[1]) describes the manner in which AChE data are used in human health risk assessment. The following text provides a brief summary of that document to provide context to points of departure selected.

AChE inhibition can be inhibited in the central or peripheral nervous tissue. Measurements of AChE or cholinesterase (ChE) inhibition in peripheral tissues (e.g., liver, diaphragm, heart, lung etc) are rare. As such, experimental laboratory studies generally measure brain (central) and blood (plasma and RBC) ChE. Blood measures do not represent the target tissue, per se, but are instead used as surrogate measures for peripheral toxicity in studies with laboratory animals or for peripheral and/or central toxicity in humans. In addition, RBC measures represent AChE, whereas plasma measures are predominately butyryl-ChE (BuChE). Thus, RBC AChE data may provide a better representation of the inhibition in target tissues. As part of the dose response assessment, evaluations of neurobehavior and clinical signs are performed to consider the dose response linkage between AChE inhibition and apical outcomes.

Refinements to OPP's use of AChE data have come in the implementation of BMD approaches in dose response assessment. Beginning with the OP CRA, OPP has increased its use of BMD modeling to derive PODs for AChE inhibiting compounds. Most often the decreasing exponential empirical model has been used.

OPP does not have a defined BMR for OPs. However, the 10% level has been used in the majority of dose response analyses conducted to date. This 10% level represents a 10% reduction in AChE activity (i.e., inhibition) compared to background (i.e., controls). Specifically, the BMD_{10} is the estimated dose where AChE is inhibited by 10% compared to background. The $BMDL_{10}$ is the lower confidence bound on the BMD_{10}.

The use of the 10% BMR is derived from a combination of statistical and biological considerations. A power analysis was conducted by the Office of Research and Development (ORD) on over 100 brain AChE datasets across more than 25 OPs as part of the OP CRA (USEPA, 2002). This analysis demonstrated that 10% is a level that can be reliably measured in the majority of rat toxicity studies. In addition, the 10% level is generally at or near the limit of sensitivity for discerning a statistically significant decrease in AChE activity in the brain compartment and is a response level close to the background brain AChE level. With respect to biological considerations, a change in 10% brain AChE inhibition is protective for downstream clinical signs and apical neurotoxic outcomes. With respect to RBC AChE inhibition, these data tend to be more variable than brain AChE data. OPP begins its BMD analyses using the 10% BMR for RBC AChE inhibition but BMRs up to 20% could be considered on a case by case basis as long as such PODs are protective for brain AChE inhibition, potential peripheral inhibition, and clinical signs of neurotoxicity.

B.2. Summary Tables of Benchmark Dose (BMD) Analyses

BMD analyses were performed with EPA's Benchmark Dose Software (Version 2.4) using an exponential model for continuous data (Bever and Holman, D435480, 9/1/2016). The data selected for evaluation consisted of decreased brain and red blood cell (RBC) cholinesterase (AChE) activities from rats in an acute comparative cholinesterase assay (CCA; MRID 48773401a). The results of the acute dosing BMD analyses are summarized below in Table B.1.

Table B.1. Results of BMD Modeling (mg/kg) for Brain and RBC ChE Data on TCVP, Acute Oral Dosing Study in Rats.

Study	Age Sex	Brain BMD_{10}	Brain $BMDL_{10}$	RBC BMD_{10}	RBC $BMDL_{10}$
MRID 48773401a Acute CCA	PND 11 Male	5.1	4.5	5.0	4.1
MRID 48773401a Acute CCA	PND 11 Female	5.9	4.8	3.4	2.8
MRID 48773401a Acute CCA	PND 21 Male	3.5	3.2	3.2	2.8

MRID 48773401a Acute CCA	PND 21 Female	5.3[a]	3.7	4.6	2.8
MRID 48773401a Acute CCA	Adult Male	7.4	5.6	6.5	3.6
MRID 48773401a Acute CCA	Adult Female	11.6[a]	9.8	14.9	11.2

CCA = Comparative Cholinesterase Assay

[a]Although the model chosen resulted in program warning that "the model may not adequately describe the data", fit was considered adequate based on similarity to values from other data sets, plausibility after considering empirical data (ground-truthing), and visual assessment of the fit.

Previously, Benchmark Dose (BMD) analyses were performed with EPA's Benchmark Dose Software (Version 2.4) using an exponential model for continuous data [2]. The Hill model was also performed for some data sets, but did not result in the best fit for the data. The data selected for evaluation consisted of decreased brain and red blood cell (RBC) cholinesterase (ChE) activities. Data were analyzed from a 21-day oral toxicity study (MRID 45570601), a 13-week subchronic oral toxicity study (MRID 43371201), a 2 year chronic oral toxicity study (MRID 42980901); a gestational comparative cholinesterase assay (MRID 48291101); and a 28-day inhalation toxicity study (MRID 48803501). The results of the repeated oral and inhalation dosing BMD analyses are summarized below in Table B.2. Good model fit ($p>0.1$) was obtained for the majority of the analyses, with any exceptions being noted.

Table B.2. Results of BMD Exponential Modeling for Brain and RBC ChE Data on TCVP, Repeated Oral Dosing Studies in Rats, Ranging in Duration from 21 days to 2 years.				
TCVP Study	Age/Sex	Compartment	BMD Results	
			BMD_{10}	$BMDL_{10}$
MRID 43371201 13W Oral – 13 Weeks	Adult Male	Brain	No dose response (analysis not performed)	
	Adult Female	Brain	No dose response	
	Adult Male	RBC	61.6 mg/kg/day	26.3 mg/kg/day
	Adult Female	RBC	10.5 mg/kg/day	8.0 mg/kg/day
MRID 42980901 Chronic Oral Tox – 364, 539, and 721 Days	Adult Female	RBC	No dose-response effect was observed at 364, 539, or 721 days	
MRID 45570601 21D Oral Tox – 21 Days	Adult Female	Brain	14.7 mg/kg/day	12.2 mg/kg/day
		RBC	9.9 mg/kg/day	6.7 mg/kg/day
MRID 48803501 28D Inhalation – 28 Days	Adult Male	RBC	0.122 mg/L	0.022 mg/L
	Adult Female	RBC	0.394 mg/L	0.050 mg/L

[1] USEPA (2000) Office of Pesticide Programs, US Environmental Protection Agency, Washington DC 20460. August 18, 2000 Office of Pesticide Programs Science Policy of the Use of Data on Cholinesterase Inhibition for Risk Assessments of Organophosphorous and Carbamate Pesticides.
[2] J. Bever. Tetrachlorvinphos: Benchmark Dose Analysis of Subchronic and Chronic Studies to Support Derivation of Points of Departure. 5/20/2014. TXR # 0056970. D420286.

Appendix C. Methodologies for HEC Calculations

The RfC methodology applies a dosimetric adjustment that takes into consideration not only the differences in ventilation rate (MV) but also the physicochemical properties of the inhaled compound, the type of toxicity observed (e.g., systemic vs. portal-of-entry) and the pharmacokinetic (PK) **but not pharmacodynamic** (PD) differences between animals and humans. Based on the EPA's RfC guidance (1994), the methodology for RfCs derivation is an estimate of the quantitative dose-response assessment of chronic non-cancer toxicity for individual inhaled chemicals and includes dosimetric adjustment to account for the species-specific relationships of exposure concentration to deposited/delivered dose. This adjustment is influenced by the physicochemical properties of the inhaled compound as well as the type of toxicity observed (e.g., systemic vs. portal-of-entry), and takes into consideration the PK differences between animals and humans. Though the RfC methodology was developed to estimate toxicity of inhaled chemicals over a lifetime, it can be used for other inhalation exposures (e.g., acute and short-term exposures) since the dosimetric adjustment incorporates mechanistic determinants of disposition that can be applied to shorter duration of exposures provided the assumptions underlying the methodology are still valid. These assumptions, in turn, vary depending on the type of toxicity observed. Thus the derivation of a HEC for inhaled gases is described by the following equation:

$$HEC = POD_{study} * \frac{D_{\text{animal exposure (hrs / day)}}}{D_{\text{human exposure (hrs / day)}}} * \frac{W_{\text{animal exposure (days / wk)}}}{W_{\text{human exposure (days / wk)}}} * RGDR$$

Where:
POD_{study}: Point of departure identified in the critical toxicology study
$D_{animal\ exposure}$: Duration of animal exposure (hrs/day; days/wk)
$D_{anticipated\ exposure}$: Anticipated human duration of exposure (hrs/day; days/wk)
RGDR: Regional Gas Dose Ratio

Calculations used to estimate the inhalation risk to humans from aerosols are dependent not on the RGDR as for gases, but on the regional deposited dose ratio (RDDR). Inhalation studies using aerosols characterize particulate exposure by defining the particulate diameter (mass median aerodynamic diameter [MMAD]) and the geometric standard deviation (σ_g), which is then used to determine the RDDR. The RDDR is a multiplicative factor used to adjust an observed inhalation particulate exposure concentration of an animal (A) to the predicted inhalation particulate exposure concentration for a human (H) that would be associated with the same dose delivered to the rth region or target tissue.

$$RDDR_r = \frac{(RDD_r/\text{Normalizing Factor})_A}{(RDD_r/\text{Normalizing Factor})_H}$$

As with calculations for gases, the r regions and potential target tissues are the three respiratory regions (ET, TB, PU). The RDDR is easily calculated by using a software program designed specifically for computing the RDDR from the MMAD and σ_g defined from an aerosol inhalation study. The values for the species-specific parameters used to calculate the RDDR are

provided in the EPA document "Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry."

Regional Deposited Dose Ratio (RDDR) for TCVP

MMAD = 2.57
Sigma g = 3.79

SPECIES	Body Weight (g)	Minute Ventilation (VE, ml)
rat	267	189.8
human	70000	13800.0

	Extrarespiratory BW (g)	deposited fraction
rat	267	0.460
human	70000	0.657
RATIO	0.004	0.700

RDDR = $(VE/BW)_{animal}/(VE/BW)_{human}$ * $deposited\ fraction_{animal}/deposited\ fraction_{human}$
= $(189.8/267)_{animal}/(13800/70000)_{human}$ * 0.460/0.657
= 2.525

The magnitude of the UFs applied is dependent on the methodology used to calculate risk. The RfC methodology takes into consideration the PK differences **but not the PD differences**. Consequently, the UF for interspecies extrapolation may be reduced to 3X (to account for the PD differences) while the UF for intraspecies variation is retained at 10X. Thus, the UF when using the RfC methodology is customarily 30X.

C.1. HEC Calculations for Residential Exposure:

Assume residents will be exposed for 24 hrs/day and 7 days/week:

*HEC = $NOAEL_{study}$ * (daily duration of $exposure_{animal}$/daily duration of $exposure_{human}$) * (days/week of $exposure_{animal}$/days/week of $exposure_{human}$) * RDDR*

*Residential Bystander HEC = 0.022 mg/L * (6/24) * (5/7) * 2.525 = 0.0099 mg/L*
*Residential Handler Outdoor HEC = 0.022 mg/L * 2.525 = 0.0555 mg/L*

Table C.1.1. HEC Array for Residential Handler Risk Assessment.												
Relevant Study		$BMDL_{10}$ (mg/L)	BMD_{10} (mg/L)	Da	Dh	Wa	Wh	RDDR	HEC (mg/L)	Inter	intra	UF
Short-& Intermediate-Term Exposure												
Inhalation – Rat (MRID 48803501) 28-day	ER	0.022	0.122	6	8	5	5	2.525	0.0555	3	10	NA
Long-Term Exposure: Not appropriate for TCVP.												

Table C.1.2. HEC Array for Residential Bystander Risk Assessment.												
Relevant Study		$BMDL_{10}$ (mg/L)	BMD_{10} (mg/L)	Da	Dh	Wa	Wh	RDDR	HEC (mg/L)	Inter	intra	UF
Short-& Intermediate-Term Exposure												
Inhalation – Rat (MRID 48803501) 28-day	ER	0.022	0.122	6	24	5	7	2.525	0.099	3	10	NA
Long-Term Exposure: Not appropriate for TCVP.												

Key for Array Tables	
LOAEL: Lowest-observed adverse-effect level	*RRDR*: Regional Deposited Dose Ratio
NOAEL: No-observed adverse-effect level	*HEC*: Human-Equivalent Concentration
Da: Daily animal exposure (hrs/day)	*inter*: Interspecies extrapolation UF
Dh: Anticipated daily human exposure (hrs/day)	*intra*: Intraspecies variation UF
Wa: Weekly animal exposure (days/week)	*UF*: Other UF(s)
Wh: Anticipated weekly human exposure (days/week)	*ER:* Extra-respiratory effects

Route-to-Route Extrapolation

More information and details in: Memo, "Route-to-Route Extrapolations" J. Whalen and H. Pettigrew, 10/10/98.

HED's route-to-route extrapolation converts human and animal values from mg/L concentrations to mg/kg oral equivalent doses. The equation uses a single conversion factor to account for default body weights and respiratory volumes. An activity factor is used to account for increased exposure resulting from increased respiration.

Using the HEC calculated (based on an increase in RBC cholinesterase inhibition in both sexes), a conversion of the inhalation concentration to a dose (mg/L to mg/kg/day) was conducted as follows:

HED (mg/kg/day) = Dose (systemic HEC value, mg/L) x A x CF (L/hr/kg) x D (hours) x AF = mg/kg

Where:

A = absorption: ratio of deposition and absorption in respiratory tract compared to absorption by the oral route.

CF = conversion factor; a L/hr/kg factor which accounts for respiratory volume and body weight for a given species and strain (Table 1 of J. Whalen and H. Pettigrew, 10/10/98).

D = duration; duration of daily animal or human exposure (hours).

AF = activity factor; animal default is 1. For humans the value varies with ventilation

**11.8 L/hr/kg is the typical breathing rate assumed for humans.*

Therefore, the residential HED for TCVP is calculated as follows:

Residential Handler HED: *(0.056 mg/L) x 11.8 L/hr/kg x 2 hr x 1 = 1.31 mg/kg/day*

C.2. HEC Calculations Occupational Exposure:

Assume workers will be exposed for 8 hrs/day and 5 days/week:

*HEC = $NOAEL_{study}$ * (daily duration of $exposure_{animal}$/daily duration of $exposure_{human}$) * (days/week of $exposure_{animal}$/days/week of $exposure_{human}$) * RDDR*

Occupational - HEC = 0.022mg/L * (6/8) * (5/5) * 2.525 = 0.0416 mg/L.

Table C.1.3. HEC Array for Occupational Risk Assessment.

Relevant Study		$BMDL_{10}$ (mg/L)	BMD_{10} (mg/L)	Da	Dh	Wa	Wh	RDDR	HEC (mg/L)	Inter	intra	UF
Short-& Intermediate-Term Exposure												
Inhalation – Rat (MRID 48803501) 28-day	ER	0.022	0.122	6	8	5	5	2.525	0.0416	3	10	NA
Long-Term Exposure: Not appropriate for TCVP.												

Key for Array Tables	
LOAEL: Lowest-observed adverse-effect level	*RRDR*: Regional Deposited Dose Ratio
NOAEL: No-observed adverse-effect level	*HEC*: Human-Equivalent Concentration
Da: Daily animal exposure (hrs/day)	*inter*: Interspecies extrapolation UF
Dh: Anticipated daily human exposure (hrs/day)	*intra*: Intraspecies variation UF
Wa: Weekly animal exposure (days/week)	*UF*: Other UF(s)
Wh: Anticipated weekly human exposure (days/week)	*ER:* Extra-respiratory effects

Route-to-Route Extrapolation

More information and details in: Memo, "Route-to-Route Extrapolations" J. Whalen and H. Pettigrew, 10/10/98.

HED's route-to-route extrapolation converts human and animal values from mg/L concentrations to mg/kg oral-equivalent doses. The equation uses a single conversion factor to account for default body weights and respiratory volumes. An activity factor is used to account for increased exposure resulting from increased respiration.

Using the HEC calculated (based on an increase in RBC cholinesterase inhibition in both sexes), a conversion of the inhalation concentration to a dose (mg/L to mg/kg/day) was conducted as follows:

HED (mg/kg/day) = Dose (systemic HEC value, mg/L) x A x CF (L/hr/kg) x D (hours) x AF = mg/kg

Where:

A	=	absorption; ratio of deposition and absorption in respiratory tract compared to absorption by the oral route.
CF	=	conversion factor; a L/hr/kg factor which accounts for respiratory volume and body weight for a given species and strain (Table 1 of J. Whalen and H. Pettigrew, 10/10/98).
D	=	duration; duration of daily animal or human exposure (hours).
AF	=	activity factor; animal default is 1. For humans, the value varies with ventilation rates

Therefore, the occupational HED for TCVP is calculated as follows:

Occupational Handler HED: 0.042 mg/L x 11.8 L/hr/kg x 1.0 x 8 hr = 3.94 mg/kg/day

Based on the current TCVP label, HED believes exposures can be short- (1-30) or intermediate- (1 to 6 months) term in duration. Long-term exposures are not anticipated for TCVP based on proposed labeled uses. For the short- and intermediate-term scenarios, inhalation data from the 28-day inhalation rodent study was most appropriate for determining HECs. In the RfC methodology, different HECs may be calculated for the same experimental NOAEL due to the following:

1. Different algorithms are used to derive HECs for systemic versus portal-of-entry effects. Typically, HECs are calculated separately for systemic versus portal-of-entry effect. For TCVP, extra-respiratory effects were observed and, therefore, only extra-respiratory HECs were derived.

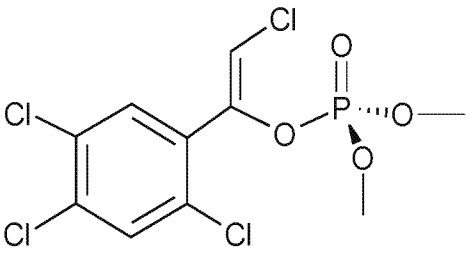
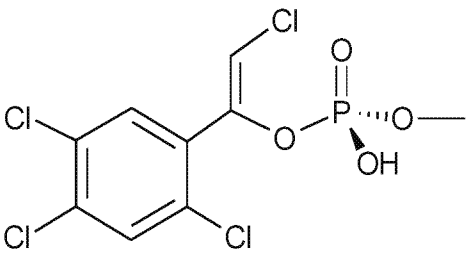
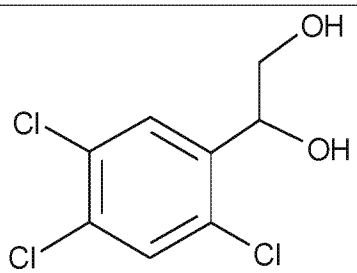
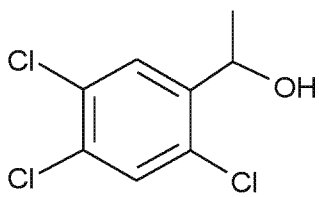
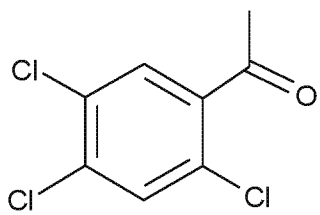
Time adjustments are traditionally needed for non-occupational (bystander) versus occupational exposure scenarios. Traditionally, HECs for non-occupational exposure are based on the number of hours an individual may be at home. Therefore, the most conservative estimate of hours spent at home would be 24 hours/day and 7 days/week. In comparison, the average workweek for an occupational worker is 8 hours/day and 5 days/week. The HEC array table reflects the time adjustment in the calculations.

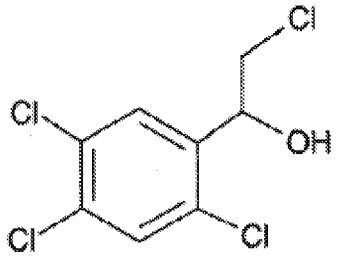
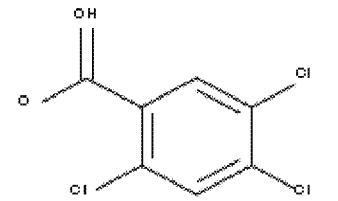
Appendix D. Physical/Chemical Properties for Tetrachlorvinphos

Table D.1 Physicochemical Properties of the Technical Grade Test Compound: Tetrachlorvinphos		
Parameter	Value	Reference [1]
Melting point/range	94.5 °C	(MRID 41222503)
pH	5.5; 1% solution	(MRID 41222503)
Density	0.83 g/mL	(MRID 41222503)
Water solubility	(25°C) 11.6 g/L	(MRID 41222503)
Solvent solubility	(mg/100mg at 25°C) chloroform 80 methanol 21 acetone 44 hexane 0.8 toluene 28	(MRID 41222503)
Vapor pressure	(25°C) 2.6 x 10^{-7} mm Hg	(MRID 41222503)
Dissociation constant, pK_a	non-ionizable	(MRID 41222503)
Octanol/water partition coefficient, Log(K_{OW})	3350 average K_{OW} at 25 °C	(MRID 41222503)
UV/visible absorption spectrum	Not available	

[1] Cited reference was reviewed under CB No. 7468, 4/3/91, R. Perfetti.

Appendix E. TCVP and Metabolites

Chemical Name	Structure	Physical/Chemical Properties[1]
Tetrachlorvinphos IUPAC: (*Z*)-2-chloro-1-(2,4,5-trichlorophenyl)vinyl dimethyl phosphate CAS: (*1Z*)-2-chloro-1-(2,4,5-trichlorophenyl)ethenyl dimethyl phosphate CAS Reg. No. 22248-79-9 COP(=O)(OC)OC(=CCl)c1cc(Cl)c(Cl)cc1Cl		Molecular weight: 365.96 g/mol VP: 2.6E-07 torr Solubility: 11.6 mg/L Log Kow: 3.53 Koc: 520-1100 L/kg$_{oc}$
Des-O-methyl tetrachlorvinphos IUPAC: (*Z*)-2-chloro-1-(2,4,5-trichlorophenyl)vinyl methyl phosphate CAS: (*1Z*)-2-chloro-1-(2,4,5-trichlorophenyl)ethenyl methyl phosphate COP(=O)(O)OC(=CCl)c1cc(Cl)c(Cl)cc1Cl		Molecular weight: 351.94 g/mol VP: 4.27E-08 torr Solubility: 3.768 mg/L Log Kow: 3.75 Koc: 702-827 L/kg$_{oc}$
1-(2,4,5-trichlorophenyl)ethanediol C(O)(CO)c1cc(Cl)c(Cl)cc1Cl		Molecular weight: 241.5 g/mol VP: 4.37E-06 torr Solubility: 250 mg/L Log Kow: 2.37 Koc: 29-36 L/kg$_{oc}$
TCPEol (SD 15509, AA849) 1-(2,4,5-trichlorophenyl)ethanol 1-(2,4,5-trichlorophenyl)ethan-1-ol CC(O)c1cc(Cl)c(Cl)cc1Cl		Molecular weight: 225.5 g/mol VP: 2.37E-04 torr Solubility: 123 mg/L Log Kow: 3.43 Koc: 319-359 L/kg$_{oc}$
TCPEone (CO300) 2,4,5-trichloroacetophenone CC(=O)c1cc(Cl)c(Cl)cc1Cl		Molecular weight: 223.5 g/mol VP: 6.32E-03 torr Solubility: 27.4 mg/L Log Kow: 3.61 Koc: 492-1,828 L/kg$_{oc}$

Chemical Name	Structure	Physical/Chemical Properties[1]
TCCEol (SD15125, AA576) l-(2,4,5-trichlorophenyl)-2-chloroethanol C(Cl)C(O)c1cc(Cl)c(Cl)cc1Cl		Molecular weight: 260 g/mol VP: 2.11E-05 torr Solubility: 250 mg/L Log Kow: 3.68 Koc: 494-608 L/kg$_{oc}$
TCBA (SD 15917) 2,4,5-Trichlorobenzoic acid C(=O)(O)c1cc(Cl)c(Cl)cc1Cl		Molecular weight: 225.5 g/mol VP: 5.52E-04 torr Solubility: 35.3 mg/L Log Kow: 3.47 Koc: 157-166 L/kg$_{oc}$

1. Physical and chemical properties for degradates obtained through EPISuite 4.11.

Appendix F. International MRLs and U.S. Tolerances

Table F.1. Tetrachlorvinphos: Summary of U.S. and International Tolerances and Maximum Residue Limits.

Commodity	U.S. Tolerances, 40 CFR §180.252 [1]		Codex MRL	Canada's MRL [2]
	Established U.S. Tolerance, ppm	Reassessed U.S. Tolerance, ppm		
Milk, fat (reflecting negligible residues in whole milk)	0.5 (of which not more than 0.05 ppm is tetrachlorvinphos *per se*)	milk: 0.1 (of which not more than 0.04 ppm is tetrachlorvinphos *per se*)	None	None
Cattle and Hog, Fat	Fat of cattle and hog: 0.2 (of which not more than 0.1 ppm is tetrachlorvinphos *per se*)	Fat of cattle and hog: 1.0 (of which not more than 0.8 ppm is tetrachlorvinphos *per se*)	None	1.5 [3]
Cattle and Hog, Muscle	meat of cattle and hog: 2.0 (of which not more than 2.0 ppm is tetrachlorvinphos *per se*)	meat of cattle and hog: 0.3 (of which not more than 0.2 ppm is tetrachlorvinphos *per se*)	None	1.5 [3]
Cattle and Hog, Kidney	kidney of cattle and hog: 1.0 (of which no more than 0.05 ppm is tetrachlorvinphos *per se*)	meat byproducts of cattle and hog : 1.0 (of which no more than 0.6 ppm is tetrachlorvinphos *per se*)	None	1.5 [3]
Cattle and Hog, Liver	liver of cattle and hog: 0.5 (of which no more than 0.05 ppm is tetrachlorvinphos *per se*)		None	1.5 [3]

Table F.1. Tetrachlorvinphos: Summary of U.S. and International Tolerances and Maximum Residue Limits.				
Commodity	U.S. Tolerances, 40 CFR §180.252 [1]		Codex MRL	Canada's MRL [2]
	Established U.S. Tolerance, ppm	Reassessed U.S. Tolerance, ppm		
Cattle and Hog, Meat byproducts	meat byproducts, except kidney and liver of cattle and hog: 1.0		None	1.5 [3]
Eggs	0.2 (of which not more than 0.05 ppm is tetrachlorvinphos *per se*)	0.3 (of which not more than 0.03 ppm is tetrachlorvinphos *per se*)	None	None
Poultry, muscle	meat of poultry: 3.0 (of which not more than 3.0 ppm is tetrachlorvinphos *per se*)	meat of poultry: 0.4 (of which not more than 0.1 ppm is tetrachlorvinphos *per se*)	None	0.75 [4]
Poultry, liver	2.0 (of which not more than 0.05 ppm is tetrachlorvinphos *per se*)	meat byproducts of poultry: 20 (of which not more than 6.0 ppm is tetrachlorvinphos *per se*)	None	0.75 [4]
Poultry, meat byproducts	meat byproducts, except liver, of poultry: 2.0	meat byproducts of poultry: 20 (of which not more than 6.0 ppm is tetrachlorvinphos *per se*)	None	0.75 [4]
Poultry, fat	7.0 (of which not more than 7.0 ppm is tetrachlorvinphos *per se*)	1.4 (of which not more than 0.1 ppm is tetrachlorvinphos *per se*)	None	0.75 [4]
Apples	None	None	None	10
Grapes	None	None	None	10

Appendix G. Summary of Residential Handler Non-Cancer Exposures and Risks

Table G.1. Residential Handler Non-cancer Dermal and Inhalation Dose Assuming a Liquid or Dust Formulation for Pet Collars.

Exposure Scenario	Reg. No.	Dermal Unit Exposure (mg/lb ai)	Inhalation Unit Exposure (mg/lb ai)	Maximum Application Rate[1] (lb ai/pet)	Amount Handled Daily[2]	Dermal Dose (mg/kg/day)[3]	Inhalation Dose (mg/kg/day)[4]
Assume Liquid Formulation -- Use of Spot-On Exposure Data (based on 2012 Residential SOPs)							
Application of TCVP Collars	2596-49: Cat	120	Negligible	0.0036: 11 gram collar	2 animals treated per day	0.0012	Negligible
	2596-50, 62: Dog			0.0061: 19 gram collar		0.0020	
				0.010: 32 gram collar		0.0034	
	2596-63: Cat			0.0048: 15 gram collar		0.0016	
				0.0055: 17 gram collar		0.0018	
	2596-83: Cat			0.0039: 12 gram collar		0.0013	
				0.0080: 25 gram collar		0.0027	
	2596-84: Dog			0.0061: 19 gram collar		0.0021	
				0.010: 32 gram collar		0.0034	
	2596-139: Cat			0.0032: 10 gram collar		0.0011	
	2596-139: Dog			0.016: 50 gram collar		0.0054	
	11556-164: Dog			0.0072: 24 gram collar		0.0024	
	11556-165:			0.0045:		0.0015	

Table G.1. Residential Handler Non-cancer Dermal and Inhalation Dose Assuming a Liquid or Dust Formulation for Pet Collars.							
Exposure Scenario	**Reg. No.**	**Dermal Unit Exposure (mg/lb ai)**	**Inhalation Unit Exposure (mg/lb ai)**	**Maximum Application Rate[1] (lb ai/pet)**	**Amount Handled Daily[2]**	**Dermal**	**Inhalation**
						Dose (mg/kg/day)[3]	**Dose (mg/kg/day)[4]**
	Cat			15 gram collar			
Assume Dust Formulation -- Use of TCVP Dust Applicator Exposure Data (MRID 45519601)							
Application of TCVP Collars	2596-49: Cat	1,700	3.1	0.0036: 11 gram collar	2 animals treated per day	0.017	0.00033
	2596-50, 62: Dog			0.0061: 19 gram collar		0.029	0.00055
				0.010: 32 gram collar		0.049	0.00092
	2596-63: Cat			0.0048: 15 gram collar		0.023	0.00043
				0.0055: 17 gram collar		0.026	0.00049
	2596-83: Cat			0.0039: 12 gram collar		0.018	0.00035
				0.0080: 25 gram collar		0.038	0.00072
	2596-84: Dog			0.0061: 19 gram collar		0.029	0.00055
				0.010: 32 gram collar		0.049	0.00092
	2596-139: Cat			0.0032: 10 gram collar		0.015	0.00029
	2596-139: Dog			0.016: 50 gram collar		0.076	0.00144
	11556-164: Dog			0.0072: 24 gram collar		0.034	0.00065
	11556-165: Cat			0.0045: 15 gram collar		0.021	0.00041

Table G.2. Residential Handler Non-cancer Risk Estimates Assuming 1/99 Liquid/Dust Ratio Formulation Pet Collars.						
Exposure Scenario	**Reg. No.**	**Maximum Application Rate[1] (lb ai/pet)**	**Amount Handled Daily[2]**	**Combined 1/99 Liquid/Dust Dermal Dose (mg/kg/day)[3]**	**Combined 1/99 Liquid/Dust Inhalation Dose (mg/kg/day)[4]**	**Combined 1/99 Liquid/Dust Ratio Inhalation MOE[5] LOC = 300**
Application of TCVP Collars	2596-49: Cat	0.0036: 11 gram collar	2 animals treated per day	0.0170	0.00032	4,100
	2596-50, 62: Dog	0.0061: 19 gram collar		0.0285	0.00054	2,400
		0.010: 32 gram collar		0.0481	0.00092	1,400
	2596-63: Cat	0.0048: 15 gram collar		0.0225	0.00043	3,100
		0.0055: 17 gram collar		0.0255	0.00049	2,700
	2596-83: Cat	0.0039: 12 gram collar		0.0180	0.00034	3,800
		0.0080: 25 gram collar		0.0376	0.00072	1,800
	2596-84: Dog	0.0061: 19 gram collar		0.0285	0.00054	2,400
		0.010: 32 gram collar		0.0481	0.00092	1,400
	2596-139: Cat	0.0032: 10 gram collar		0.0150	0.00029	4,600
	2596-139: Dog	0.016: 50 gram collar		0.0751	0.00143	920
	11556-164: Dog	0.0072: 24 gram collar		0.0338	0.00064	2,000
	11556-165: Cat	0.0045: 15 gram collar		0.0211	0.00040	3,300

1 Based on registered TCVP pet product labels.
2 Based on HED's 2012 Residential SOPs (http://www2.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide).
3 Combined 1/99 Liquid/Dust Dermal Dose = (Liquid dermal dose * 0.01) + (Dust dermal dose * 0.99)

4 Combined 1/99 Liquid/Dust Inhalation Dose = (Liquid dermal dose * 0.01) + (Dust dermal dose * 0.99)
5. No dermal MOE estimated due to lack of dermal hazard. Inhalation MOE = Inhalation HED (1.31 mg/kg/day) ÷ Combined 1/99 Liquid/Dust Inhalation Dose (mg/kg/day)

Table G.3. Residential Handler Non-cancer Risk Estimates Assuming 50/50 Liquid/Dust Ratio Formulation Pet Collars.						
Exposure Scenario	**Reg. No.**	**Maximum Application Rate[1] (lb ai/pet)**	**Amount Handled Daily[2]**	**Combined 50/50 Liquid/Dust Dermal Dose (mg/kg/day)[3]**	**Combined 50/50 Liquid/Dust Inhalation Dose (mg/kg/day)[4]**	**Combined 50/50 Liquid/Dust Ratio Inhalation MOE[5] LOC = 300**
Application of TCVP Collars	2596-49: Cat	0.0036: 11 gram collar	2 animals treated per day	0.0092	0.00016	8,000
	2596-50, 62: Dog	0.0061: 19 gram collar		0.0154	0.00028	4,800
		0.010: 32 gram collar		0.0260	0.00046	2,800
	2596-63: Cat	0.0048: 15 gram collar		0.0122	0.00022	6,000
		0.0055: 17 gram collar		0.0138	0.00025	5,300
	2596-83: Cat	0.0039: 12 gram collar		0.0097	0.00017	7,600
		0.0080: 25 gram collar		0.0203	0.00036	3,600
	2596-84: Dog	0.0061: 19 gram collar		0.0154	0.00028	4,800
		0.010: 32 gram collar		0.0260	0.00046	2,800
	2596-139: Cat	0.0032: 10 gram collar		0.0081	0.00014	9,100
	2596-139: Dog	0.016: 50 gram collar		0.0406	0.00072	1,800
	11556-164: Dog	0.0072: 24 gram collar		0.0183	0.00033	4,000
	11556-165:	0.0045:		0.0114	0.00020	6,400

Table G.3. Residential Handler Non-cancer Risk Estimates Assuming 50/50 Liquid/Dust Ratio Formulation Pet Collars.						
Exposure Scenario	**Reg. No.**	**Maximum Application Rate[1] (lb ai/pet)**	**Amount Handled Daily[2]**	**Combined 50/50 Liquid/Dust Dermal Dose (mg/kg/day)[3]**	**Combined 50/50 Liquid/Dust Inhalation Dose (mg/kg/day)[4]**	**Combined 50/50 Liquid/Dust Ratio Inhalation MOE[5] LOC = 300**
	Cat	15 gram collar				

1 Based on registered TCVP pet product labels.
2 Based on HED's 2012 Residential SOPs (http://www2.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide).
3 Combined 50/50 Liquid/Dust Dermal Dose = (Liquid dermal dose * 0.5) + (Dust dermal dose * 0.5)
4 Combined 50/50 Liquid/Dust Inhalation Dose = (Liquid dermal dose * 0.5) + (Dust dermal dose * 0.5)
5. No dermal MOE estimated due to lack of dermal hazard. Inhalation MOE = Inhalation HED (1.31 mg/kg/day) ÷ Combined 50/50 Liquid/Dust Inhalation Dose (mg/kg/day)

Table G.4. Residential Handler Non-cancer Risk Estimates Assuming 99/1 Liquid/Dust Ratio Formulation Pet Collars.						
Exposure Scenario	**Reg. No.**	**Maximum Application Rate[1] (lb ai/pet)**	**Amount Handled Daily[2]**	**Combined 99/1 Liquid/Dust Dermal Dose (mg/kg/day)[3]**	**Combined 99/1 Liquid/Dust Inhalation Dose (mg/kg/day)[4]**	**Combined 99/1 Liquid/Dust Ratio Inhalation MOE[5] LOC = 300**
Application of TCVP Collars	2596-49: Cat	0.0036: 11 gram collar	2 animals treated per day	0.0014	3.27E-06	400,000
	2596-50, 62: Dog	0.0061: 19 gram collar		0.0023	5.49E-06	240,000
		0.010: 32 gram collar		0.0039	9.25E-06	140,000
	2596-63: Cat	0.0048: 15 gram collar		0.0018	4.33E-06	300,000
		0.0055: 17 gram collar		0.0021	4.91E-06	270,000
	2596-83: Cat	0.0039: 12 gram collar		0.0015	3.47E-06	380,000
		0.0080: 25 gram collar		0.0030	7.22E-06	180,000
	2596-84: Dog	0.0061: 19 gram collar		0.0023	5.49E-06	240,000
		0.010:		0.0039	9.25E-06	140,000

Table G.4. Residential Handler Non-cancer Risk Estimates Assuming 99/1 Liquid/Dust Ratio Formulation Pet Collars.						
Exposure Scenario	**Reg. No.**	**Maximum Application Rate[1] (lb ai/pet)**	**Amount Handled Daily[2]**	**Combined 99/1 Liquid/Dust Dermal Dose (mg/kg/day)[3]**	**Combined 99/1 Liquid/Dust Inhalation Dose (mg/kg/day)[4]**	**Combined 99/1 Liquid/Dust Ratio Inhalation MOE[5] LOC = 300**
		32 gram collar				
	2596-139: Cat	0.0032: 10 gram collar		0.0012	2.89E-06	450,000
	2596-139: Dog	0.016: 50 gram collar		0.0061	1.44E-05	91,000
	11556-164: Dog	0.0072: 24 gram collar		0.0027	6.51E-06	200,000
	11556-165: Cat	0.0045: 15 gram collar		0.0017	4.07E-06	320,000

1 Based on registered TCVP pet product labels.
2 Based on HED's 2012 Residential SOPs (http://www2.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide).
3 Combined 99/1 Liquid/Dust Dermal Dose = (Liquid dermal dose * 0.99) + (Dust dermal dose * 0.01)
4 Combined 99/1 Liquid/Dust Inhalation Dose = (Liquid dermal dose * 0.99) + (Dust dermal dose * 0.01)
5. No dermal MOE estimated due to lack of dermal hazard. Inhalation MOE = Inhalation HED (1.31 mg/kg/day) ÷ Combined 99/1 Liquid/Dust Inhalation Dose (mg/kg/day)

Table G.5. Residential Handler Non-cancer Exposure and Risk Estimates from Use of TCVP Dust/Powder and Pump/Trigger Spray Products. Inhalation LOC is an MOE = 300; No dermal hazard.										
Exposure Scenario	**Reg. No.**	**Level of Concern**	**Dermal Unit Exposure (mg/lb ai)**	**Inhalation Unit Exposure (mg/lb ai)**	**Maximum Application Rate[1] (lb ai/pet)**	**Amount Handled Daily[2]**	**Dermal**		**Inhalation**	
							Dose (mg/kg/day)[3]	**MOE[4]**	**Dose (mg/kg/day)[5]**	**MOE[6]**
Application of TCVP Dusts/Powders	47000-123: Dog	Inhalation: 300	1,700	3.1	0.00037: small	2 animals treated per day	0.0018	N/A, No Dermal Hazard	0.000034	39,000
					0.00094: medium		0.0044		0.000084	16,000
					0.0015: large		0.0071		0.00013	9,700
	47000-123: Cat				0.000094: small		0.00044		0.0000084	160,000
					0.00023: medium		0.0011		0.000020	65,000

Table G.5. Residential Handler Non-cancer Exposure and Risk Estimates from Use of TCVP Dust/Powder and Pump/Trigger Spray Products. Inhalation LOC is an MOE = 300; No dermal hazard.

Exposure Scenario	Reg. No.	Level of Concern	Dermal Unit Exposure (mg/lb ai)	Inhalation Unit Exposure (mg/lb ai)	Maximum Application Rate[1] (lb ai/pet)	Amount Handled Daily[2]	Dermal		Inhalation	
							Dose (mg/kg/day)[3]	MOE[4]	Dose (mg/kg/day)[5]	MOE[6]
					0.00034: large		0.0016		0.000030	43,000
	2596-78: Cat				0.00062: small		0.0029		0.000056	24,000
					0.0010: large		0.0049		0.000093	14,000
	2596-79; Dog				0.0010: small		0.0049		0.000093	14,000
					0.0021: medium		0.0097		0.00019	7,100
					0.0026: large		0.0122		0.00023	5,600
	67517-82: Dog				0.0011: small		0.0053		0.00010	13,000
					0.0028: medium		0.013		0.00025	5,200
					0.0045: large		0.021		0.00040	3,200
	67517-82: Cat				0.00028: small		0.0013		0.000025	52,000
					0.00067: medium		0.0032		0.000061	22,000
					0.0010: large		0.0048		0.000091	14,000
Application of TCVP Pump/Trigger Sprays	2596-126, -140: Cat (Trigger)		820	3.3	0.00055: small		0.0013	N/A, No Dermal Hazard	0.000053	25000
					0.00077: medium		0.0018		0.000074	18000
	2596-140 Cat (Pump)				0.00011: small		0.00026		0.000011	120,000
					0.00016: large		0.00036		0.000015	87,000

Table G.5. Residential Handler Non-cancer Exposure and Risk Estimates from Use of TCVP Dust/Powder and Pump/Trigger Spray Products. Inhalation LOC is an MOE = 300; No dermal hazard.

Exposure Scenario	Reg. No.	Level of Concern	Dermal Unit Exposure (mg/lb ai)	Inhalation Unit Exposure (mg/lb ai)	Maximum Application Rate[1] (lb ai/pet)	Amount Handled Daily[2]	Dermal		Inhalation	
							Dose (mg/kg/day)[3]	MOE[4]	Dose (mg/kg/day)[5]	MOE[6]
	2596-125, -140: Dog (Trigger)				0.00077: small		0.0018		0.000074	18,000
					0.00088: medium		0.0020		0.000084	16,000
					0.0015: large		0.0035		0.00015	8,900

1 Based on registered TCVP pet product labels.
2 Based on HED's 2012 Residential SOPs (http://www2.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide)
3 Dermal Dose = Dermal Unit Exposure (mg/lb ai) × Application Rate (lb ai/pet) × Area Treated or Amount Handled (pets/day) × Dermal Absorption Factor (9.6 %) ÷ Body Weight (69 kg). Dermal dose presented only for purpose of calculation of cancer risks for residential handlers.
4 No dermal MOE estimated due to lack of dermal hazard.
5 Inhalation Dose = Inhalation Unit Exposure (mg/lb ai) × Application Rate (lb ai/pet) × Area Treated or Amount Handled (pets/day) ÷ Body Weight (69 kg).
6 Inhalation MOE = Inhalation HED (1.31 mg/kg/day) ÷ Inhalation Dose (mg/kg/day).

Appendix H. Summary of Residential Handler Cancer Exposure and Risk Estimates

Table H.1. Residential Handler Cancer Exposure and Risk Estimates from TCVP Pet Collar Products Using 1/99 Liquid/Dust Formulation Approach.

Reg No./ Animal Type	Animal Size	Lifestage	Liquid LADD[1]	Dust LADD[2]	1/99 Liquid/Dust Cancer Risk Estimate[3]
2596-49: Cat	Any	Adult	8.5E-06	1.2E-04	2.2E-07
2596-50, 62: Dog	Small		1.4E-05	2.1E-04	3.7E-07
	Medium, Large		2.4E-05	3.5E-04	6.3E-07
2596-63: Cat	Small		1.1E-05	1.6E-04	3.0E-07
	Medium, Large		1.3E-05	1.8E-04	3.3E-07
2596-83: Cat	Small		9.0E-06	1.3E-04	2.4E-07
	Medium, Large		1.9E-05	2.7E-04	4.9E-07
2596-84: Dog	Small		1.4E-05	2.1E-04	3.7E-07
	Medium, Large		2.4E-05	3.5E-04	6.3E-07
2596-139: Cat	Any		7.5E-06	1.1E-04	2.0E-07
2596-139: Dog	Any		3.8E-05	5.4E-04	9.8E-07
11556-164: Dog	Any		1.7E-05	2.4E-04	4.4E-07
11556-165: Cat	Any		1.1E-05	1.5E-04	2.8E-07

1 Liquid LADD = [Inhalation + Dermal Dose (mg/kg/day)] × [Days per year of exposure (days/yr) ÷ 365 days/year] × [Years per lifetime of exposure (yrs) ÷ Lifetime expectancy (yrs)]. Inhalation exposures considered negligible based on use of spot-on data for liquid pet collar formulation.

2 Dust LADD = [Inhalation + Dermal Dose (mg/kg/day)] × [Days per year of exposure (days/yr) ÷ 365 days/year] × [Years per lifetime of exposure (yrs) ÷ Lifetime expectancy (yrs)].

3 Cancer risk estimates = [(Liquid LADD * 0.01) + (Dust LADD * 0.99)] × Q_1^*, where $Q_1^* = 1.83 \times 10^{-3}$ $(mg/kg/day)^{-1}$

Table H.2. Residential Handler Cancer Exposure and Risk Estimates from TCVP Pet Collar Products Using 50/50 Liquid/Dust Formulation Approach

Reg No./ Animal Type	Animal Size	Lifestage	Liquid LADD[1]	Dust LADD[2]	50/50 Liquid/Dust Cancer Risk Estimate[3]
2596-49: Cat	Any	Adult	8.5E-06	1.2E-04	1.2E-07

Table H.2. Residential Handler Cancer Exposure and Risk Estimates from TCVP Pet Collar Products Using 50/50 Liquid/Dust Formulation Approach					
Reg No./ Animal Type	**Animal Size**	**Lifestage**	**Liquid LADD[1]**	**Dust LADD[2]**	**50/50 Liquid/Dust Cancer Risk Estimate[3]**
2596-50, 62: Dog	Small		1.4E-05	2.1E-04	2.0E-07
	Medium, Large		2.4E-05	3.5E-04	3.4E-07
2596-63: Cat	Small		1.1E-05	1.6E-04	1.6E-07
	Medium, Large		1.3E-05	1.8E-04	1.8E-07
2596-83: Cat	Small		9.0E-06	1.3E-04	1.3E-07
	Medium, Large		1.9E-05	2.7E-04	2.7E-07
2596-84: Dog	Small		1.4E-05	2.1E-04	2.0E-07
	Medium, Large		2.4E-05	3.5E-04	3.4E-07
2596-139: Cat	Any		7.5E-06	1.1E-04	1.1E-07
2596-139: Dog	Any		3.8E-05	5.4E-04	5.3E-07
11556-164: Dog	Any		1.7E-05	2.4E-04	2.4E-07
11556-165: Cat	Any		1.1E-05	1.5E-04	1.5E-07

1 Liquid LADD = [Inhalation + Dermal Dose (mg/kg/day)] × [Days per year of exposure (days/yr) ÷ 365 days/year] × [Years per lifetime of exposure (yrs) ÷ Lifetime expectancy (yrs)]. Inhalation exposures considered negligible based on use of spot-on data for liquid pet collar formulation.

2 Dust LADD = [Inhalation + Dermal Dose (mg/kg/day)] × [Days per year of exposure (days/yr) ÷ 365 days/year] × [Years per lifetime of exposure (yrs) ÷ Lifetime expectancy (yrs)].

3 Cancer risk estimates = [(Liquid LADD * 0.5) + (Dust LADD * 0.5)] × Q_1^*, where $Q_1^* = 1.83 \times 10^{-3}$ $(mg/kg/day)^{-1}$

Table H.3. Residential Handler Cancer Exposure and Risk Estimates from TCVP Pet Collar Products Using 99/1 Liquid/Dust Formulation Approach					
Reg No./ Animal Type	**Animal Size**	**Lifestage**	**Liquid LADD[1]**	**Dust LADD[2]**	**50/50 Liquid/Dust Cancer Risk Estimate[3]**
2596-49: Cat	Any	Adult	8.5E-06	1.2E-04	1.8E-08
2596-50, 62: Dog	Small		1.4E-05	2.1E-04	3.0E-08
	Medium, Large		2.4E-05	3.5E-04	5.0E-08
2596-63: Cat	Small		1.1E-05	1.6E-04	2.3E-08
	Medium, Large		1.3E-05	1.8E-04	2.7E-08

Table H.3. Residential Handler Cancer Exposure and Risk Estimates from TCVP Pet Collar Products Using 99/1 Liquid/Dust Formulation Approach					
Reg No./ Animal Type	**Animal Size**	**Lifestage**	**Liquid LADD[1]**	**Dust LADD[2]**	**50/50 Liquid/Dust Cancer Risk Estimate[3]**
2596-83: Cat	Small		9.0E-06	1.3E-04	1.9E-08
	Medium, Large		1.9E-05	2.7E-04	3.9E-08
2596-84: Dog	Small		1.4E-05	2.1E-04	3.0E-08
	Medium, Large		2.4E-05	3.5E-04	5.0E-08
2596-139: Cat	Any		7.5E-06	1.1E-04	1.6E-08
2596-139: Dog	Any		3.8E-05	5.4E-04	7.8E-08
11556-164: Dog	Any		1.7E-05	2.4E-04	3.5E-08
11556-165: Cat	Any		1.1E-05	1.5E-04	2.2E-08

1 Liquid LADD = [Inhalation + Dermal Dose (mg/kg/day)] × [Days per year of exposure (days/yr) ÷ 365 days/year] × [Years per lifetime of exposure (yrs) ÷ Lifetime expectancy (yrs)]. Inhalation exposures considered negligible based on use of spot-on data for liquid pet collar formulation.

2 Dust LADD = [Inhalation + Dermal Dose (mg/kg/day)] × [Days per year of exposure (days/yr) ÷ 365 days/year] × [Years per lifetime of exposure (yrs) ÷ Lifetime expectancy (yrs)].

3 Cancer risk estimates = [(Liquid LADD * 0.99) + (Dust LADD * 0.01)] × Q_1^*, where $Q_1^* = 1.83 \times 10^{-3}$ $(mg/kg/day)^{-1}$

Table H.4. Residential Handler Dermal and Inhalation Cancer Exposure and Risk Estimates from TCVP Pet Products				
Reg No./ Animal Type	**Animal Size**	**Lifestage**	**Total LADD[1,2]**	**Cancer Risk Estimate[3]**
Dust/Powder				
47000-123: Dog	Small	Adult	1.9E-05	3.5E-08
	Medium		4.7E-05	8.7E-08
	Large		7.6E-05	1.4E-07
47000-123: Cat	Small		4.7E-06	8.7E-09
	Medium		1.1E-05	2.1E-08
	Large		1.7E-05	3.1E-08
2596-78: Cat	Small		3.1E-05	5.7E-08
	Medium		5.2E-05	9.6E-08

Table H.4. Residential Handler Dermal and Inhalation Cancer Exposure and Risk Estimates from TCVP Pet Products				
Reg No./ Animal Type	**Animal Size**	**Lifestage**	**Total LADD[1,2]**	**Cancer Risk Estimate[3]**
2596-79: Dog	Small		5.2E-05	9.6E-08
	Medium		1.0E-04	1.9E-07
	Large		1.3E-04	2.4E-07
67517-82: Dog	Small		5.7E-05	1.0E-07
	Medium		1.4E-04	2.6E-07
	Large		2.3E-04	4.2E-07
67517-82: Cat	Small		1.4E-05	2.6E-08
	Medium		3.4E-05	6.2E-08
	Large		5.1E-05	9.4E-08
Pump/Trigger Sprays				
2596-126: -140: Cat (Trigger)	Small	Adult	1.4E-05	2.5E-08
	Large		1.9E-05	3.5E-08
2596-140: Cat (Pump)	Small		2.8E-06	5.1E-09
	Large		3.9E-06	7.2E-09
2596-125, -140: Dog (Trigger)	Small		1.9E-05	3.5E-08
	Medium		2.2E-05	4.0E-08
	Large		3.9E-05	7.0E-08

1 Total Lifetime Average Daily Dose (LADD, mg/kg/day) = Dermal LADD (mg/kg/day) + Inhalation LADD (mg/kg/day).
2 Dermal and Inhalation LADD equations provided in Appendix B.
3 Cancer risk estimates = Total LADD × Q_1^*, where $Q_1^* = 1.83 \times 10^{-3}$ $(mg/kg/day)^{-1}$

Appendix I. Summary of Residential Post-Application Non-Cancer Exposure and Risk Estimates

Table I.1. Residential Post-application Non-cancer Incidental Oral Dose Assuming a Liquid or Dust Formulation for Pet Collars.

Animal Type	Animal Size	Application Rate (mg ai)	$F_{aihands}$	DE	SA_H	HR	F_m	ET	Replenish-ment interval (min)	N_Replen	SE	Freq_HtM	Incidental oral Absorbed Dose (mg/kg/day)
				Dermal Exposure (mg)	Surface area of 1 hand (cm^2)	Hand residue loading (mg/cm^2)	Fraction of hand mouthed	Exposure Time (hours/day)		# replenish-ment intervals per hour (intervals/hr)	Fraction Saliva Extraction	Number of hand-to-mouth contacts events per hour (events/hr)	
Assume Liquid Formulation -- Use of Davis Study (2008) and Liquid TCs													
Cat (2596-49)	small	1650	0.04	6.1	150	0.0008	0.13	1	15	4	0.48	20	0.0056
	medium	1650	0.04	3.7	150	0.0005	0.13	1	15	4	0.48	20	0.0033
	large	1650	0.04	2.3	150	0.0003	0.13	1	15	4	0.48	20	0.0021
Dog (2596-50,62)	small	2774	0.04	5.1	150	0.0007	0.13	1	15	4	0.48	20	0.0047
	large	4672	0.04	2.4	150	0.0003	0.13	1	15	4	0.48	20	0.0021
Cat (2596-83)	small	1752	0.04	6.5	150	0.0009	0.13	1	15	4	0.48	20	0.0059
	large	3650	0.04	5.1	150	0.0007	0.13	1	15	4	0.48	20	0.0046
Cat (2596-139)	small	1460	0.04	5.4	150	0.0007	0.13	1	15	4	0.48	20	0.0049
	medium	1460	0.04	3.2	150	0.0004	0.13	1	15	4	0.48	20	0.0030
	large	1460	0.04	2.0	150	0.0003	0.13	1	15	4	0.48	20	0.0018
Dog (11556-164)	small	3288	0.04	6.1	150	0.0008	0.13	1	15	4	0.48	20	0.0055
	medium	3288	0.04	2.6	150	0.0003	0.13	1	15	4	0.48	20	0.0024
	large	3288	0.04	1.7	150	0.0002	0.13	1	15	4	0.48	20	0.0015
Cat (11556-165)	small	2055	0.04	7.6	150	0.0010	0.13	1	15	4	0.48	20	0.0069
	medium	2055	0.04	4.6	150	0.0006	0.13	1	15	4	0.48	20	0.0042
	large	2055	0.04	2.9	150	0.0004	0.13	1	15	4	0.48	20	0.0026
Dog (2596-84)	small	2774	0.04	5.1	150	0.0007	0.13	1	15	4	0.48	20	0.0047
	large	4672	0.04	2.4	150	0.0003	0.13	1	15	4	0.48	20	0.0021
Dog (2596-139)	small	7300	0.04	13.5	150	0.0018	0.13	1	15	4	0.48	20	0.0123
	medium	7300	0.04	5.8	150	0.0008	0.13	1	15	4	0.48	20	0.0053
	large	7300	0.04	3.7	150	0.0005	0.13	1	15	4	0.48	20	0.0034
Cat (2596-63)	small	2190	0.04	8.1	150	0.0011	0.13	1	15	4	0.48	20	0.0074
	large	2482	0.04	3.5	150	0.0005	0.13	1	15	4	0.48	20	0.0031
Assume Dust Formulation -- Use of Davis Study (2008) and Dust TCs													
Cat (2596-49)	small	1650	0.37	166	150	0.2049	0.13	1	15	4	0.48	20	1.40
	medium	1650	0.37	100	150	0.1229	0.13	1	15	4	0.48	20	0.84
	large	1650	0.37	62	150	0.0768	0.13	1	15	4	0.48	20	0.52
Dog (2596-50,62)	small	2774	0.37	140	150	0.1723	0.13	1	15	4	0.48	20	1.18
	large	4672	0.37	64	150	0.0791	0.13	1	15	4	0.48	20	0.54
Cat (2596-83)	small	1752	0.37	176	150	0.2176	0.13	1	15	4	0.48	20	1.48

Table I.1. Residential Post-application Non-cancer Incidental Oral Dose Assuming a Liquid or Dust Formulation for Pet Collars.

Animal Type	Animal Size	Application Rate (mg ai)	$F_{aihands}$	DE	SA_H	HR	F_m	ET	Replenish-ment interval (min)	N_Replen	SE	Freq_HtM	Incidental oral Absorbed Dose (mg/kg/day)
				Dermal Exposure (mg)	Surface area of 1 hand (cm^2)	Hand residue loading (mg/cm^2)	Fraction of hand mouthed	Exposure Time (hours/day)		# replenish-ment intervals per hour (intervals/hr)	Fraction Saliva Extraction	Number of hand-to-mouth contacts events per hour (events/hr)	
	large	3650	0.37	138	150	0.1700	0.13	1	15	4	0.48	20	1.16
Cat (2596-139)	small	1460	0.37	147	150	0.1813	0.13	1	15	4	0.48	20	1.24
	medium	1460	0.37	88	150	0.1088	0.13	1	15	4	0.48	20	0.74
	large	1460	0.37	55	150	0.0680	0.13	1	15	4	0.48	20	0.46
Dog (11556-164)	small	3288	0.37	166	150	0.2042	0.13	1	15	4	0.48	20	1.39
	medium	3288	0.37	71	150	0.0875	0.13	1	15	4	0.48	20	0.60
	large	3288	0.37	45	150	0.0557	0.13	1	15	4	0.48	20	0.38
Cat (11556-165)	small	2055	0.37	207	150	0.2552	0.13	1	15	4	0.48	20	1.74
	medium	2055	0.37	124	150	0.1531	0.13	1	15	4	0.48	20	1.04
	large	2055	0.37	78	150	0.0957	0.13	1	15	4	0.48	20	0.65
Dog (2596-84)	small	2774	0.37	140	150	0.1723	0.13	1	15	4	0.48	20	1.18
	large	4672	0.37	64	150	0.0791	0.13	1	15	4	0.48	20	0.54
Dog (2596-139)	small	7300	0.37	368	150	0.4533	0.13	1	15	4	0.48	20	3.09
	medium	7300	0.37	158	150	0.1943	0.13	1	15	4	0.48	20	1.33
	large	7300	0.37	100	150	0.1236	0.13	1	15	4	0.48	20	0.84
Cat (2596-63)	small	2190	0.37	221	150	0.2720	0.13	1	15	4	0.48	20	1.86
	large	2482	0.37	94	150	0.1156	0.13	1	15	4	0.48	20	0.79

1. Application rates are label defined. Refer to D426984.
2. Dermal Exposure (mg/day) = [Transfer Coefficient (cm^2/hr)] * [Application Rate (label defined) * Fraction Application Rate (0.0040; Davis, M. Et. al) ÷ Surface Area of Cat/Dog (Cat: Small, 1,500; Medium, 2,500; Large, 4,000 cm^2 - Dog: Small, 3,000; Medium, 7,000; Large, 11,000 cm^2)] x [Exposure Time (Adults, 0.77 hours/day; Children, 1.0 hours/day))
3. Incidental Oral Dose (mg/kg/day) = [Hand Residue Loading (mg/cm^2)] × [Fraction of Hand Mouthed (0.13) × Surface Area of 1 Child Hand (150 cm^2)] x [Exposure Time (1.0 hrs/day) × # of Replenishment Intervals/hr (4 int/hr)) × (1-((1-Saliva Extraction Factor (0.5))^(Number of Hand-to-Mouth Events per Hour (20 events/hr)) ÷ (# of Replenishment Intervals/hr))] / [Body Weight (11 kg child 1 to < 2 years old years old)]
   Where the Hand Residue Loading (mg/cm^2) = [Fai_{hands} (Solid, 0.37; Liquids; 0.040) x Dermal Exposure (mg/day)] ÷ [Surface Area of 1 Child Hand (150 cm^2) x 2]

Table I.2. Residential Post-Application Non-Cancer Incidental Oral Exposure Estimates from TCVP Pet Collars. 1/99 Ratio Liquid to Dust/Solid Formulation. Incidental Oral LOC is an MOE = 1,000.

EPA Reg. No./ Animal	Lifestage	Application Rate (mg ai)[1]	Animal Size	Liquid HtM Dose (mg/kg/day)[2]	Dust HtM Dose (mg/kg/day)[3]	1/99 Liquid/Dust Combined MOE[4]
2596-49: Cat	Children 1 < 2	1,650	Small	0.00557	1.39768	**2**
			Medium	0.00334	0.83861	**3.4**
			Large	0.00209	0.52413	**5.4**
2596-50, 62: Dog	Children 1 < 2	2,770	Small	0.00468	1.17504	**2.4**
		4,670	Large	0.00215	0.53973	**5.2**
2596-83: Cat	Children 1 < 2	1,750	Small	0.00591	1.48427	**1.9**
		3,650	Large	0.00462	1.15958	**2.4**
2596-139: Cat	Children 1 < 2	3,650	Small	0.00493	1.23689	**2.3**
			Medium	0.00296	0.74213	**3.8**
			Large	0.00185	0.46383	**6.1**
11556-164: Dog	Children 1 < 2	3,290	Small	0.00555	1.39277	**2**
			Medium	0.00238	0.59690	**4.7**
			Large	0.00151	0.37985	**7.4**
11556-165: Cat	Children 1 < 2	2,060	Small	0.00693	1.74096	**1.6**
			Medium	0.00416	1.04458	**2.7**
			Large	0.00260	0.65286	**4.3**
2596-84: Dog	Children 1 < 2	2,770	Small	0.00468	1.17504	**2.4**
		4,670	Large	0.00215	0.53973	**5.2**
2596-139: Dog	Children 1 < 2	7,300	Small	0.01232	3.09222	**0.91**
			Medium	0.00528	1.32524	**2.1**
			Large	0.00336	0.84333	**3.4**
2596-63: Cat	Children 1 < 2	2,190	Small	0.00739	1.85533	**1.5**
		2,480	Large	0.00314	0.78852	**3.6**

1. Application rates are label defined. Refer to D426984.
2. Liquid and Dust HTM Doses from Table E.1
3. 1/99 Liquid/Dust Combined MOE = Incidental Oral NOAEL (2.8 mg/kg/day) ÷ [(Liquid HtM Dose * 0.01) + (Dust HtM Dose * 0.99)]. Bolded MOEs indicate a risk of concern.

Table I.3. Residential Post-Application Non-Cancer Incidental Oral Exposure Estimates from TCVP Pet Collars. 50/50 Ratio Liquid to Dust/Solid Formulation. Incidental Oral LOC is an MOE = 1,000.

EPA Reg. No./ Animal	Lifestage	Application Rate (mg ai)[1]	Animal Size	Liquid HtM Dose (mg/kg/day)[2]	Dust HtM Dose (mg/kg/day)[3]	50/50 Liquid/Dust Combined MOE[4]
2596-49: Cat	Children 1 < 2	1,650	Small	0.00557	1.39768	**4**
			Medium	0.00334	0.83861	**6.7**
			Large	0.00209	0.52413	**11**
2596-50, 62: Dog	Children 1 < 2	2,770	Small	0.00468	1.17504	**4.7**
		4,670	Large	0.00215	0.53973	**10**
2596-83: Cat	Children 1 < 2	1,750	Small	0.00591	1.48427	**3.8**
		3,650	Large	0.00462	1.15958	**4.8**
2596-139: Cat	Children 1 < 2	3,650	Small	0.00493	1.23689	**4.5**
			Medium	0.00296	0.74213	**7.5**
			Large	0.00185	0.46383	**12**
11556-164: Dog	Children 1 < 2	3,290	Small	0.00555	1.39277	**4**
			Medium	0.00238	0.59690	**9.3**
			Large	0.00151	0.37985	**15**
11556-165: Cat	Children	2,060	Small	0.00693	1.74096	**3.2**

Table I.3. Residential Post-Application Non-Cancer Incidental Oral Exposure Estimates from TCVP Pet Collars. 50/50 Ratio Liquid to Dust/Solid Formulation. Incidental Oral LOC is an MOE = 1,000.

EPA Reg. No./ Animal	Lifestage	Application Rate (mg ai)[1]	Animal Size	Liquid HtM Dose (mg/kg/day)[2]	Dust HtM Dose (mg/kg/day)[3]	50/50 Liquid/Dust Combined MOE[4]
	1 < 2		Medium	0.00416	1.04458	**5.3**
			Large	0.00260	0.65286	**8.5**
2596-84: Dog	Children 1 < 2	2,770	Small	0.00468	1.17504	**4.7**
		4,670	Large	0.00215	0.53973	**10**
2596-139: Dog	Children 1 < 2	7,300	Small	0.01232	3.09222	**1.8**
			Medium	0.00528	1.32524	**4.2**
			Large	0.00336	0.84333	**6.6**
2596-63: Cat	Children 1 < 2	2,190	Small	0.00739	1.85533	**3**
		2,480	Large	0.00314	0.78852	**7.1**

1. Application rates are label defined. Refer to D426984.
2. Liquid and Dust HTM Doses from Table E.1
3. 1/99 Liquid/Dust Combined MOE = Incidental Oral NOAEL (2.8 mg/kg/day) ÷ [(Liquid HtM Dose * 0.5) + (Dust HtM Dose * 0.5)]. Bolded MOEs indicate a risk of concern.

Table I.4. Residential Post-Application Non-Cancer Incidental Oral Exposure Estimates from TCVP Pet Collars. 99/1 Ratio Liquid to Dust/Solid Formulation. Incidental Oral LOC is an MOE = 1,000.

EPA Reg. No./ Animal	Lifestage	Application Rate (mg ai)[1]	Animal Size	Liquid HtM Dose (mg/kg/day)[2]	Dust HtM Dose (mg/kg/day)[3]	99/1 Liquid/Dust Combined MOE[4]
2596-49: Cat	Children 1 < 2	1,650	Small	0.00557	1.39768	**140**
			Medium	0.00334	0.83861	**240**
			Large	0.00209	0.52413	**380**
2596-50, 62: Dog	Children 1 < 2	2,770	Small	0.00468	1.17504	**170**
		4,670	Large	0.00215	0.53973	**370**
2596-83: Cat	Children 1 < 2	1,750	Small	0.00591	1.48427	**140**
		3,650	Large	0.00462	1.15958	**170**
2596-139: Cat	Children 1 < 2	3,650	Small	0.00493	1.23689	**160**
			Medium	0.00296	0.74213	**270**
			Large	0.00185	0.46383	**430**
11556-164: Dog	Children 1 < 2	3,290	Small	0.00555	1.39277	**140**
			Medium	0.00238	0.59690	**340**
			Large	0.00151	0.37985	**530**
11556-165: Cat	Children 1 < 2	2,060	Small	0.00693	1.74096	**120**
			Medium	0.00416	1.04458	**190**
			Large	0.00260	0.65286	**310**
2596-84: Dog	Children 1 < 2	2,770	Small	0.00468	1.17504	**170**
		4,670	Large	0.00215	0.53973	**370**
2596-139: Dog	Children 1 < 2	7,300	Small	0.01232	3.09222	**65**
			Medium	0.00528	1.32524	**150**
			Large	0.00336	0.84333	**240**
2596-63: Cat	Children 1 < 2	2,190	Small	0.00739	1.85533	**110**
		2,480	Large	0.00314	0.78852	**250**

1. Application rates are label defined. Refer to D426984.
2. Liquid and Dust HTM Doses from Table E.1
3. 1/99 Liquid/Dust Combined MOE = Incidental Oral NOAEL (2.8 mg/kg/day) ÷ [(Liquid HtM Dose * 0.99) + (Dust HtM Dose * 0.01)]. Bolded MOEs indicate a risk of concern.

Table I.5. Residential Post-Application Non-Cancer Exposure and Risk Estimates from TCVP Dust/Powder and Pump/Trigger Spray Formulations. Incidental Oral LOC is an MOE = 1,000

EPA Reg. No./ Animal	Lifestage	Application Rate (mg ai)[1]	Animal Size	Dermal Exposure (mg/day)[2]	Incidental Oral Dose (mg/kg/day)[3]	MOE[4]
Dusts/Powders						
47000-123: Dog	Children 1 < 2	170	Small	1.0	0.0087	**320**
		430	Medium	1.1	0.0093	**300**
		680	Large	1.1	0.0095	**300**
47000-123: Cat	Children 1 < 2	43	Small	0.52	0.0043	**640**
		100	Medium	0.74	0.0063	**450**
		150	Large	0.70	0.0059	**480**
2596-78: Cat	Children 1 < 2	280	Small	3.4	0.0287	**98**
		470	Large	2.1	0.0180	**160**
2596-79: Dog	Children 1 < 2	470	Small	2.9	0.0240	**120**
		940	Medium	2.4	0.0205	**140**
		1,200	Large	1.9	0.0163	**170**
67517-82: Dog	Children 1 < 2	510	Small	3.1	0.0261	**110**
		1,300	Medium	3.3	0.0280	**100**
		2,000	Large	3.4	0.0285	**98**
67517-82: Cat	Children 1 < 2	130	Small	1.6	0.0130	**210**
		310	Medium	2.2	0.0188	**150**
		460	Large	2.1	0.0176	**160**
Pump/Trigger Sprays						
2596-126, 140: Cat (Trigger)	Children 1 < 2	250	Small	1.9	0.00172	1,600
		350	Large	0.99	0.00090	3,100
2596-140: Cat (Pump)	Children 1 < 2	51	Small	0.39	0.00035	8,000
		71	Large	0.20	0.00018	15,000
2596-125, -140: Dog (Trigger)	Children 1 < 2	350	Small	1.3	0.00120	2,300
		400	Medium	0.65	0.00059	4,800
		700	Large	0.72	0.00066	4,300

1. Application rates are label defined. Refer to D426984.
2. Dermal Exposure (mg/day) = [Transfer Coefficient (cm^2/hr)] * [Application Rate (label defined) * Fraction Application Rate (Dust, 0.00048; Spray, 0.0081) ÷ Surface Area of Cat/Dog (Cat: Small, 1,500; Medium, 2,500; Large, 4,000 cm^2 - Dog: Small, 3,000; Medium, 7,000; Large, 11,000 cm^2)] x [Exposure Time (Adults, 0.77 hours/day; Children, 1.0 hours/day))]
3. Incidental Oral Dose (mg/kg/day) = [Hand Residue Loading (mg/cm^2)] × [Fraction of Hand Mouthed (0.13) × Surface Area of 1 Child Hand (150 cm^2)] x [Exposure Time (1.0 hrs/day) × # of Replenishment Intervals/hr (4 int/hr)) × (1-((1-Saliva Extraction Factor (0.5))^(Number of Hand-to-Mouth Events per Hour (20 events/hr)) ÷ (# of Replenishment Intervals/hr))] / [Body Weight (11 kg child 1 to < 2 years old years old)]
   Where the Hand Residue Loading (mg/cm^2) = [Fai_{hands} (Dusts, 0.37; Liquids; 0.040) x Dermal Exposure (mg/day)] ÷ [Surface Area of 1 Child Hand (150 cm^2) x 2]
4. MOE = Incidental Oral NOAEL (2.8 mg/kg/day) ÷ Incidental Oral Dose (mg/kg/day). Bolded MOEs indicate a risk of concern.

Appendix J. Summary of Residential Post-Application Cancer Exposure and Risks

Table J.1. Residential Post-Application Cancer Exposure and Risk Estimates from TCVP Pet Collar – 1/99 Ratio of Liquid/Dust Formulation						
Animal Type	**Animal Size**	**Lifestage**	**Liquid LADD[1]**	**Dust LADD[2]**	**Combined 1/99 Liquid/Dust LADD[3]**	**Cancer Risk Estimate[4]**
Exposure Data Source: Davis, M., et al (2008)						
2596-49: Cat	Small	Adult	5.8E-03	1.6E-01	1.5E-01	2.8E-04
	Medium		3.5E-03	9.4E-02	9.3E-02	1.7E-04
	Large		2.2E-03	5.8E-02	5.8E-02	1.1E-04
2596-50,62: Dog	Small		4.9E-03	1.3E-01	1.3E-01	2.4E-04
	Large		2.2E-03	6.0E-02	6.0E-02	1.1E-04
2596-83: Cat	Small		6.2E-03	1.7E-01	1.6E-01	3.0E-04
	Large		4.8E-03	1.3E-01	1.3E-01	2.3E-04
2596-139: Cat	Small		5.1E-03	1.4E-01	1.4E-01	2.5E-04
	Medium		3.1E-03	8.3E-02	8.2E-02	1.5E-04
	Large		1.9E-03	5.2E-02	5.1E-02	9.4E-05
11556-164: Dog	Small		5.8E-03	1.6E-01	1.5E-01	2.8E-04
	Medium		2.5E-03	6.7E-02	6.6E-02	1.2E-04
	Large		1.6E-03	4.2E-02	4.2E-02	7.7E-05
11556-165: Cat	Small		7.2E-03	1.9E-01	1.9E-01	3.5E-04
	Medium		4.3E-03	1.2E-01	1.2E-01	2.1E-04
	Large		2.7E-03	7.3E-02	7.2E-02	1.3E-04
2596-84: Dog	Small		4.9E-03	1.3E-01	1.3E-01	2.4E-04
	Large		2.2E-03	6.0E-02	6.0E-02	1.1E-04
2596-139: Dog	Small		1.3E-02	3.5E-01	3.4E-01	6.3E-04
	Medium		5.5E-03	1.5E-01	1.5E-01	2.7E-04
	Large		3.5E-03	9.4E-02	9.3E-02	1.7E-04
2596-63: Cat	Small		7.7E-03	2.1E-01	2.1E-01	3.8E-04
	Large		3.3E-03	8.8E-02	8.7E-02	1.6E-04

1 Liquid LADD = [Dermal Dose (mg/kg/day)] × [Days per year of exposure (days/yr) ÷ 365 days/year] × [Years per lifetime of exposure (yrs) ÷ Lifetime expectancy (yrs)].

2 Dust LADD = [Dermal Dose (mg/kg/day)] × [Days per year of exposure (days/yr) ÷ 365 days/year] × [Years per lifetime of exposure (yrs) ÷ Lifetime expectancy (yrs)]
3 Combined 1/99 Liquid/Dust LADD = (Liquid LADD * 0.01) + (Dust LADD * 0.99)
4 Cancer risk estimates = Combined 1/99 Liquid/Dust LADD × Q_1^*, where $Q_1^* = 1.83 \times 10^{-3}$ $(mg/kg/day)^{-1}$

Table J.2. Residential Post-Application Cancer Exposure and Risk Estimates from TCVP Pet Collar - 50/50 Ratio of Liquid and Solid Formulation

Animal Type	Animal Size	Lifestage	Liquid LADD[1]	Dust LADD[2]	Combined 50/50 Liquid/Dust LADD[3]	Cancer Risk Estimate[4]
2596-49: Cat	Small	Adult	2.9E-03	7.8E-02	8.1E-02	1.5E-04
	Medium		1.7E-03	4.7E-02	4.9E-02	8.9E-05
	Large		1.1E-03	2.9E-02	3.0E-02	5.5E-05
2596-50,62: Dog	Small		2.4E-03	6.6E-02	6.8E-02	1.2E-04
	Large		1.1E-03	3.0E-02	3.1E-02	5.7E-05
2596-83: Cat	Small		3.1E-03	8.3E-02	8.6E-02	1.6E-04
	Large		2.4E-03	6.5E-02	6.7E-02	1.2E-04
2596-139: Cat	Small		2.6E-03	6.9E-02	7.2E-02	1.3E-04
	Medium		1.5E-03	4.1E-02	4.3E-02	7.9E-05
	Large		9.6E-04	2.6E-02	2.7E-02	4.9E-05
11556-164: Dog	Small		2.9E-03	7.8E-02	8.1E-02	1.5E-04
	Medium		1.2E-03	3.3E-02	3.5E-02	6.3E-05
	Large		7.9E-04	2.1E-02	2.2E-02	4.0E-05
11556-165: Cat	Small		3.6E-03	9.7E-02	1.0E-01	1.8E-04
	Medium		2.2E-03	5.8E-02	6.0E-02	1.1E-04
	Large		1.4E-03	3.6E-02	3.8E-02	6.9E-05
2596-84: Dog	Small		2.4E-03	6.6E-02	6.8E-02	1.2E-04
	Large		1.1E-03	3.0E-02	3.1E-02	5.7E-05
2596-139: Dog	Small		6.4E-03	1.7E-01	1.8E-01	3.3E-04
	Medium		2.7E-03	7.4E-02	7.7E-02	1.4E-04
	Large		1.7E-03	4.7E-02	4.9E-02	8.9E-05
2596-63: Cat	Small		3.8E-03	1.0E-01	1.1E-01	2.0E-04
	Large		1.6E-03	4.4E-02	4.6E-02	8.3E-05

1 Liquid LADD = [Dermal Dose (mg/kg/day)] × [Days per year of exposure (days/yr) ÷ 365 days/year] × [Years per lifetime of exposure (yrs) ÷ Lifetime expectancy (yrs)].

2 Dust LADD = [Dermal Dose (mg/kg/day)] × [Days per year of exposure (days/yr) ÷ 365 days/year] × [Years per lifetime of exposure (yrs) ÷ Lifetime expectancy (yrs)]
3 Combined 50/50 Liquid/Dust LADD = (Liquid LADD * 0.5) + (Dust LADD * 0.5)
4 Cancer risk estimates = Combined 50/50 Liquid/Dust LADD × Q_1^*, where $Q_1^* = 1.83 \times 10^{-3}$ $(mg/kg/day)^{-1}$

Table J.3. Residential Post-Application Cancer Exposure and Risk Estimates from TCVP Pet Collar - 99/1 Ratio of Liquid and Solid Formulation

Animal Type	Animal Size	Lifestage	Liquid LADD[1]	Dust LADD[2]	Combined 99/1 Liquid/Dust LADD[3]	Cancer Risk Estimate[4]
2596-49: Cat	Small	Adult	5.7E-03	1.6E-03	7.3E-03	1.3E-05
	Medium		3.4E-03	9.4E-04	4.4E-03	8.0E-06
	Large		2.2E-03	5.8E-04	2.7E-03	5.0E-06
2596-50,62: Dog	Small		4.8E-03	1.3E-03	6.1E-03	1.1E-05
	Large		2.2E-03	6.0E-04	2.8E-03	5.2E-06
2596-83: Cat	Small		6.1E-03	1.7E-03	7.7E-03	1.4E-05
	Large		4.8E-03	1.3E-03	6.1E-03	1.1E-05
2596-139: Cat	Small		5.1E-03	1.4E-03	6.5E-03	1.2E-05
	Medium		3.0E-03	8.3E-04	3.9E-03	7.1E-06
	Large		1.9E-03	5.2E-04	2.4E-03	4.4E-06
11556-164: Dog	Small		5.7E-03	1.6E-03	7.3E-03	1.3E-05
	Medium		2.4E-03	6.7E-04	3.1E-03	5.7E-06
	Large		1.6E-03	4.2E-04	2.0E-03	3.6E-06
11556-165: Cat	Small		7.1E-03	1.9E-03	9.1E-03	1.7E-05
	Medium		4.3E-03	1.2E-03	5.5E-03	1.0E-05
	Large		2.7E-03	7.3E-04	3.4E-03	6.2E-06
2596-84: Dog	Small		4.8E-03	1.3E-03	6.1E-03	1.1E-05
	Large		2.2E-03	6.0E-04	2.8E-03	5.2E-06
2596-139: Dog	Small		1.3E-02	3.5E-03	1.6E-02	3.0E-05
	Medium		5.4E-03	1.5E-03	6.9E-03	1.3E-05
	Large		3.5E-03	9.4E-04	4.4E-03	8.1E-06
2596-63: Cat	Small		7.6E-03	2.1E-03	9.7E-03	1.8E-05
	Large		3.2E-03	8.8E-04	4.1E-03	7.5E-06

1 Liquid LADD = [Dermal Dose (mg/kg/day)] × [Days per year of exposure (days/yr) ÷ 365 days/year] × [Years per lifetime of exposure (yrs) ÷ Lifetime expectancy (yrs)].
2 Dust LADD = [Dermal Dose (mg/kg/day)] × [Days per year of exposure (days/yr) ÷ 365 days/year] × [Years per lifetime of exposure (yrs) ÷ Lifetime expectancy (yrs)]
3 Combined 99/1 Liquid/Dust LADD = (Liquid LADD * 0.99) + (Dust LADD * 0.01)

4 Cancer risk estimates = Combined 99/1 Liquid/Dust LADD × Q_1^*, where Q_1^* = 1.83 x 10^{-3} (mg/kg/day)$^{-1}$

Table J.4. Residential Post-Application Cancer Exposure and Risk Estimates from TCVP Pet Products				
Animal Type	**Animal Size**	**Lifestage**	**LADD[1,2]**	**Cancer Risk Estimate[3]**
Dust/Powder				
47000-123: Dog	Small	Adult	5.9E-04	1.1E-06
	Medium		6.3E-04	1.2E-06
	Large		6.4E-04	1.2E-06
47000-123: Cat	Small		2.9E-04	5.4E-07
	Medium		4.2E-04	7.8E-07
	Large		4.0E-04	7.3E-07
2596-78: Cat	Small		1.9E-03	3.6E-06
	Large		1.2E-03	2.2E-06
2596-79: Dog	Small		1.6E-03	3.0E-06
	Medium		1.4E-03	2.5E-06
	Large		1.1E-03	2.0E-06
67517-82: Dog	Small		1.8E-03	3.2E-06
	Medium		1.9E-03	3.5E-06
	Large		1.9E-03	3.5E-06
67517-82: Cat	Small		8.8E-04	1.6E-06
	Medium		1.3E-03	2.3E-06
	Large		1.2E-03	2.2E-06
Pump/Trigger Spray				
2596-126, 140: Cat (Trigger)	Small	Adult	5.3E-04	9.6E-07
	Large		2.8E-04	5.1E-07
2596-140: Cat (Pump)	Small		1.1E-04	2.0E-07
	Large		5.6E-05	1.0E-07
2596-125, -140: Dog (Trigger)	Small		3.7E-04	6.7E-07
	Medium		1.8E-04	3.3E-07
	Large		2.0E-04	3.7E-07

1 Total Lifetime Average Daily Dose (mg/kg/day) = Dermal LADD (mg/kg/day) + Inhalation LADD (mg/kg/day).
2 Dermal and Inhalation LADD equations provided in Appendix B.
3 Cancer risk estimates = Total LADD × Q1*, where Q1* = 1.83 x 10^{-3} (mg/kg/day)$^{-1}$

Appendix K. Summary of Occupational Handler Non-Cancer Exposures and Risks

Table K.1. TCVP Occupational Handler Non-Cancer Risk Estimates.											
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Inhalation Dose (mg/kg/day)**				**Inhalation MOEs (LOC is an MOE = 300)** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario.			
				No R	**PF5 R**	**PF10 R**	**EC**	**No R**	**PF5 R**	**PF10 R**	**EC**
Mixer/Loaders											
(1a) Mixing/ Loading Liquids for Groundboom Applications	Poultry Buildings (Floors)	0.00077 lb ai/sq ft	100,000 (sq ft/day)	2.5E-04	4.9E-05	2.5E-05	9.3E-05	16,000	81,000	160,000	43,000
	Poultry Buildings (Floor Management, Fowl Tick)	0.00064 lb ai/sq ft		2.0E-04	4.1E-05	2.0E-05	7.7E-05	19,000	97,000	190,000	51,000
	Poultry Buildings (Flies Residual)	0.00013 lb ai/sq ft		4.1E-05	8.3E-06	4.1E-06	1.6E-05	95,000	480,000	950,000	250,000
	Poultry Floor Management	0.000064 lb ai/sq ft		2.0E-05	4.1E-06	2.0E-06	7.7E-06	190,000	970,000	1,900,000	510,000
(1b) Mixing/ Loading Liquids for Paint Applications	Poultry Buildings (Roost)	0.077 lb ai/gallon	2 gallons	4.9E-07	9.8E-08	4.9E-08	1.9E-07	8.1E+06	4.0E+07	8.1E+07	2.1E+07
		0.064 lb ai/gallon		4.1E-07	8.1E-08	4.1E-08	1.5E-07	9.7E+06	4.8E+07	9.7E+07	2.6E+07
(2a) Mixing/ Loading Wettable Powders for Groundboom Applications	Poultry Buildings (Including: Droppings, Floor Management Litter, Fowl Tick)	0.00080 lb ai/sq ft	100,000 sq ft	0.050	0.010	0.0050	0.00028	**79**	400	790	14,000
	Dairy Barns, Poultry Houses, Swine Barns, or Other Animal Buildings	0.00032 lb ai/sq ft		0.020	0.040	0.0020	0.00011	**200**	990	2,000	35,000
(2b) Mixing/ Loading Wettable Powders for Paint Applications	Poultry (Floor Management – Roost)	0.080 lb ai/gallon	2 gallons	1.0E-04	2.0E-05	1.0E-05	5.6E-07	40,000	200,000	400,000	7,100,000
(3a) Mixing/ Loading Dusts for		0.030 lb ai/gallon		3.7E-05	7.5E-06	3.7E-06	2.1E-07	110,000	530,000	1,100,000	1.9E+07

Table K.1. TCVP Occupational Handler Non-Cancer Risk Estimates.											
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Inhalation Dose (mg/kg/day)**				**Inhalation MOEs (LOC is an MOE = 300)** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario.			
				No R	**PF5 R**	**PF10 R**	**EC**	**No R**	**PF5 R**	**PF10 R**	**EC**
Paint Applications (WP Data as Surrogate)											
Applicators											
(4) Groundboom Applications	Poultry Buildings (Including: Droppings, Floor Management Litter, Fowl Tick, Garbage Piles, Manure Piles, Under Feed Troughs)	0.00080 lb ai/sq ft	100,000 sq ft	3.9E-04	7.9E-05	3.9E-05	5.0E-05	10,000	50,000	100,000	79,000
	Poultry Buildings (Including: Ceilings, Floors, Larvicide, Walls)	0.00077 lb ai/sq ft		3.8E-04	7.6E-05	3.8E-05	4.8E-05	10,000	52,000	100,000	82,000
	Poultry Buildings (Including: Floor Management, Fowl Tick, Larvicide)	0.00064 lb ai/sq ft		3.2E-04	6.3E-05	3.2E-05	4.0E-05	12,000	63,000	120,000	99,000
	Dairy Barns, Poultry Houses, Swine Barns, or Other Animal Buildings	0.00032 lb ai/sq ft		1.6E-04	3.2E-05	1.6E-05	2.0E-05	25,000	120,000	250,000	200,000
	Poultry Buildings (Flies Residual)	0.00013 lb ai/sq ft		6.4E-05	1.3E-05	6.4E-06	8.1E-06	61,000	310,000	610,000	490,000
	Poultry (Floor Management)	0.000064 lb ai/sq ft		3.2E-05	6.3E-06	3.2E-06	4.0E-06	120,000	630,000	1,200,000	990,000
(5) Open Pour Liquid Additive for	Cattle Feed (Concentrate)	0.0039 lb ai/animal	1,000 cows	1.2E-05	2.5E-06	1.2E-06	No Data	320,000	1,600,000	3,200,000	No Data
	Cattle Feed (Concentrate)	0.0022 lb ai/animal		7.0E-06	1.4E-06	7.0E-07	No Data	560,000	2,800,000	5,600,000	No Data

Table K.1. TCVP Occupational Handler Non-Cancer Risk Estimates.											
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Inhalation Dose (mg/kg/day)**				**Inhalation MOEs (LOC is an MOE = 300)** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario.			
				No R	**PF5 R**	**PF10 R**	**EC**	**No R**	**PF5 R**	**PF10 R**	**EC**
Feed Through Applications	Horse Feed	0.0017 lb ai/animal	500 horses	2.7E-06	5.4E-07	2.7E-07	No Data	1,500,000	7,300,000	15,000,000	No Data
	Swine Feed	0.00060 lb ai/animal	6,250 pigs	1.2E-05	2.4E-06	1.2E-06	No Data	330,000	1,700,000	3,300,000	No Data
(6a) RTU Pet Collars - 1/99 liquid/dust ratio	Cat (2596-49)	0.0036 lb ai/animal	8 animals	0.0072	0.0014	0.00072	No Data	550	2,700	5,500	No Data
	Dog (2596-50,62) - Small	0.0061 lb ai/animal		0.012	0.0025	0.0012	No Data	320	1,600	3,200	No Data
	Dog (2596-50,62) - Large	0.010 lb ai/animal		0.020	0.0040	0.0020	No Data	**200**	980	2,000	No Data
	Cat (2596-63) - Small	0.0048 lb ai/animal		0.0096	0.0019	0.00096	No Data	410	2,100	4,100	No Data
	Cat (2596-63) - Large	0.0055 lb ai/animal		0.011	0.0022	0.0011	No Data	360	1,800	3,600	No Data
	Cat (2596-83) - Small	0.0039 lb ai/animal		0.0078	0.0016	0.00078	No Data	500	2,500	5,000	No Data
	Cat (2596-83) - Large	0.0080 lb ai/animal		0.016	0.0032	0.0016	No Data	**250**	1,200	2,500	No Data
	Dog (2596-84) – Small	0.0061 lb ai/animal		0.012	0.0025	0.0012	No Data	320	1,600	3,200	No Data
	Dog (2596-84) – Large	0.010 lb ai/animal		0.020	0.0040	0.0020	No Data	**200**	980	2,000	No Data
	Cat (2596-139) - All	0.0032 lb ai/animal		0.0064	0.0013	0.00064	No Data	610	3,100	6,100	No Data
	Dog (2596-139) - All	0.016 lb ai/animal		0.032	0.0064	0.0032	No Data	**120**	610	1,200	No Data
	Dog (11556-164) - All	0.0072 lb ai/animal		0.014	0.0029	0.0014	No Data	**270**	1,400	2,700	No Data
	Cat (11556-165) - All	0.0045 lb ai/animal		0.0090	0.0018	0.00090	No Data	440	2,200	4,400	No Data
(6b) RTU Pet Collars - 50/50	Cat (2596-49)	0.0036 lb ai/animal		0.0037	0.00073	0.00037	No Data	1,100	5,400	11,000	No Data
	Dog (2596-50,62) - Small	0.0061 lb ai/animal		0.0062	0.0012	0.00062	No Data	640	3,200	6,400	No Data

Table K.1. TCVP Occupational Handler Non-Cancer Risk Estimates.												
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Inhalation Dose (mg/kg/day)**				**Inhalation MOEs (LOC is an MOE = 300)** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario.			
				No R	**PF5 R**	**PF10 R**	**EC**	**No R**	**PF5 R**	**PF10 R**	**EC**
liquid/dust ratio	Dog (2596-50,62) - Large	0.010 lb ai/animal		0.010	0.0020	0.0010	No Data	390	1,900	3,900	No Data
	Cat (2596-63) - Small	0.0048 lb ai/animal		0.0049	0.00097	0.00049	No Data	810	4,100	8,100	No Data
	Cat (2596-63) - Large	0.0055 lb ai/animal		0.0056	0.0011	0.00056	No Data	700	3,500	7,000	No Data
	Cat (2596-83) - Small	0.0039 lb ai/animal		0.0040	0.00079	0.00040	No Data	1,000	5,000	10,000	No Data
	Cat (2596-83) - Large	0.0080 lb ai/animal		0.0081	0.0016	0.00081	No Data	490	2,400	4,900	No Data
	Dog (2596-84) – Small	0.0061 lb ai/animal		0.0062	0.0012	0.00062	No Data	640	3,200	6,400	No Data
	Dog (2596-84) – Large	0.010 lb ai/animal		0.010	0.0020	0.0010	No Data	390	1,900	3,900	No Data
	Cat (2596-139) - All	0.0032 lb ai/animal		0.0032	0.00065	0.00032	No Data	1,200	6,100	12,000	No Data
	Dog (2596-139) - All	0.016 lb ai/animal		0.016	0.0032	0.0016	No Data	**240**	1,200	2,400	No Data
	Dog (11556-164) - All	0.0072 lb ai/animal		0.0073	0.001465	0.00073	No Data	540	2,700	5,400	No Data
	Cat (11556-165) - All	0.0045 lb ai/animal		0.0046	0.00092	0.00046	No Data	860	4,300	8,600	No Data
(6c) RTU Pet Collars - 99/1 liquid/dust ratio	Cat (2596-49)	0.0036 lb ai/animal		0.000073	0.000015	0.0000073	No Data	54,000	270,000	540,000	No Data
	Dog (2596-50,62) - Small	0.0061 lb ai/animal		0.00012	0.000025	0.000012	No Data	32,000	160,000	320,000	No Data
	Dog (2596-50,62) - Large	0.010 lb ai/animal		0.00020	0.000041	0.000020	No Data	19,000	97,000	190,000	No Data
	Cat (2596-63) - Small	0.0048 lb ai/animal		0.000097	0.000019	0.000010	No Data	40,000	200,000	400,000	No Data
	Cat (2596-63) - Large	0.0055 lb ai/animal		0.00011	0.000022	0.000011	No Data	35,000	180,000	350,000	No Data
	Cat (2596-83) - Small	0.0039 lb ai/animal		0.000079	0.000016	0.0000079	No Data	50,000	250,000	500,000	No Data

Table K.1. TCVP Occupational Handler Non-Cancer Risk Estimates.												
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Inhalation Dose (mg/kg/day)**				**Inhalation MOEs (LOC is an MOE = 300)** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario.			
				No R	**PF5 R**	**PF10 R**	**EC**	**No R**	**PF5 R**	**PF10 R**	**EC**
	Cat (2596-83) - Large	0.0080 lb ai/animal		0.00016	0.000033	0.000016	No Data	24,000	120,000	240,000	No Data
	Dog (2596-84) – Small	0.0061 lb ai/animal		0.00012	0.000025	0.000012	No Data	32,000	160,000	320,000	No Data
	Dog (2596-84) – Large	0.010 lb ai/animal		0.00020	0.000041	0.000020	No Data	19,000	97,000	190,000	No Data
	Cat (2596-139) - All	0.0032 lb ai/animal		0.000065	0.000013	0.0000065	No Data	61,000	300,000	610,000	No Data
	Dog (2596-139) - All	0.016 lb ai/animal		0.00033	0.000065	0.000033	No Data	12,000	61,000	120,000	No Data
	Dog (11556-164) - All	0.0072 lb ai/animal		0.00015	0.000029	0.000015	No Data	27,000	130,000	270,000	No Data
	Cat (11556-165) - All	0.0045 lb ai/animal		0.000091	0.000018	0.0000091	No Data	43,000	220,000	430,000	No Data
(7) RTU Dust/Powder Applications	Dog (47000-123) - Small	0.00037 lb ai/animal		0.00075	0.00015	0.000075	No Data	5,200	26,000	52,000	5,200
	Dog (47000-123) - Medium	0.00094 lb ai/animal		0.0019	0.00038	0.00019	No Data	2,100	10,000	21,000	2,100
	Dog (47000-123) - Large	0.0015 lb ai/animal		0.0030	0.00061	0.00030	No Data	1,300	6,500	13,000	1,300
	Cat (47000-123) - Small	0.000090 lb ai/animal		0.00018	0.000037	0.000018	No Data	22,000	110,000	220,000	22,000
	Cat (47000-123) - Medium	0.00022 lb ai/animal		0.00045	0.000089	0.000045	No Data	8,800	44,000	88,000	8,800
	Cat (47000-123) - Large	0.00034 lb ai/animal		0.00069	0.00014	0.000069	No Data	5,700	29,000	57,000	5,700
	Cat (2596-78) - Small	0.00062 lb ai/animal		0.0013	0.00025	0.00013	No Data	3,100	16,000	31,000	3,100
	Cat (2596-78) - Large	0.0010 lb ai/animal		0.0020	0.00041	0.00020	No Data	1,900	9,700	19,000	1,900
	Dog (2596-79) - Small	0.0010 lb ai/animal		0.0020	0.00041	0.00020	No Data	1,900	9,700	19,000	No Data
	Dog (2596-79) - Medium	0.0021 lb ai/animal		0.0043	0.00085	0.00043	No Data	920	4,600	9,200	No Data

Table K.1. TCVP Occupational Handler Non-Cancer Risk Estimates.												
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Inhalation Dose (mg/kg/day)**				**Inhalation MOEs (LOC is an MOE = 300)** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario.			
				No R	**PF5 R**	**PF10 R**	**EC**	**No R**	**PF5 R**	**PF10 R**	**EC**
	Dog (2596-79) - Large	0.0026 lb ai/animal		0.0053	0.0011	0.00053	No Data	750	3,700	7,500	No Data
	Dog (67517-82) - Small	0.0011 lb ai/animal		0.0022	0.00045	0.00022	No Data	1,800	8,800	18,000	No Data
	Dog (67517-82) - Medium	0.0028 lb ai/animal		0.0057	0.0011	0.00057	No Data	690	3,500	6,900	No Data
	Dog (67517-82) - Large	0.0045 lb ai/animal		0.0091	0.0018	0.00091	No Data	430	2,200	4,300	No Data
	Cat (67517-82) - Small	0.00028 lb ai/animal		0.00057	0.00011	0.000057	No Data	6,900	35,000	69,000	No Data
	Cat (67517-82) - Medium	0.00067 lb ai/animal		0.0014	0.00027	0.00014	No Data	2,900	14,000	29,000	No Data
	Cat (67517-82) - Large	0.0010 lb ai/animal		0.0020	0.00041	0.00020	No Data	1,900	9,700	19,000	No Data
(8) RTU Pump/Trigger Spray Applications	Cat (2596-126,140) - Trigger -Small	0.00055 lb ai/animal		0.00021	0.000042	0.000021	No Data	19,000	94,000	190,000	No Data
	Cat (2596-126,140) - Trigger - Large	0.00077 lb ai/animal		0.00029	0.000059	0.000029	No Data	13,000	67,000	130,000	No Data
	Cat (2596-140) - Pump - Small	0.00011 lb ai/animal		0.000042	0.0000084	0.0000042	No Data	94,000	470,000	940,000	No Data
	Cat (2596-140) - Pump - Large	0.00016 lb ai/animal		0.000061	0.000012	0.0000061	No Data	64,000	320,000	640,000	No Data
	Dog (2596-125,-140) - Small	0.00077 lb ai/animal		0.00029	0.000059	0.000029	No Data	13,000	67,000	130,000	No Data
	Dog (2596-125,-140) - Medium	0.00088 lb ai/animal		0.00034	0.000067	0.000034	No Data	12,000	58,000	120,000	No Data
	Dog (2596-125,-140) - Large	0.0015 lb ai/animal		0.00057	0.00012	0.000057	No Data	6,900	34,000	69,000	No Data
Mixers/Loaders/Applicators											
(9a) Liquid: Backpack Sprayer	Beef Cattle - Direct Applied	0.039 lb ai/animal	400 animals	0.0068	0.0014	0.00068	No Data	580	2,900	5,800	No Data
		0.032 lb ai/animal		0.0056	0.0011	0.00056	No Data	710	3,500	7,100	No Data
	Woody Borders of Kennels, Yards,	0.032 lb ai/sq ft	1,000 sq ft	0.014	0.0028	0.0014	No Data	**280**	1,400	2,800	No Data

Table K.1. TCVP Occupational Handler Non-Cancer Risk Estimates.											
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Inhalation Dose (mg/kg/day)**				**Inhalation MOEs (LOC is an MOE = 300)** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario.			
				No R	**PF5 R**	**PF10 R**	**EC**	**No R**	**PF5 R**	**PF10 R**	**EC**
	Campgrounds, Recreational Parks, Footpaths and Roadways		(spot)								
	Beef Cattle - Direct Applied	0.026 lb ai/animal	400 animals	0.0045	0.00090	0.00045	No Data	870	4,400	8,700	No Data
	Swine - Direct Applied	0.049 lb ai/animal		0.0085	0.0017	0.00085	No Data	460	2,300	4,600	No Data
	Lactating Dairy Cattle - Direct Applied	0.0049 lb ai/animal		0.00085	0.00017	0.000085	No Data	4,600	23,000	46,000	No Data
		0.0013 lb ai/animal		0.00023	0.000045	0.000023	No Data	17,000	87,000	170,000	No Data
	Poultry Buildings (Walls, Ceilings, Floors, Larvicide)	0.00077 lb ai/sq ft	20,000 sq ft	0.0067	0.0013	0.00067	No Data	590	2,900	5,900	No Data
	Poultry Buildings (Floor Management, Fowl Tick, Larvicide)	0.00064 lb ai/sq ft		0.0056	0.0011	0.00056	No Data	710	3,500	7,100	No Data
	Poultry (Caged) - Direct Applied	0.00032 lb ai/bird	20,000 birds	0.0028	0.00056	0.00028	No Data	1,400	7,100	14,000	No Data
	Poultry Buildings (Flies Residual) -	0.00013 lb ai/sq ft	20,000 sq ft	0.0011	0.00023	0.00011	No Data	3,500	17,000	35,000	No Data
	Poultry (Chicken on Litter) - Direct Applied	0.000078 lb ai/bird	20,000 birds	0.00068	0.00014	0.000068	No Data	5,800	29,000	58,000	No Data
	Poultry Floor Management	0.000064 lb ai/sq ft	20,000 sq ft	0.00056	0.00011	0.000056	No Data	7,100	35,000	71,000	No Data
(9b) Liquid: Manually-Pressurized Handwand	Beef Cattle - Direct Applied	0.039 lb ai/animal	400 animals	0.0068	0.0014	0.00068	No Data	580	2,900	5,800	No Data
		0.032 lb ai/animal		0.0056	0.0011	0.00056	No Data	710	3,500	7,100	No Data
	Woody Borders of Kennels, Yards, Campgrounds,	0.032 lb ai/sq ft	1,000 sq ft (spot)	0.0139	0.0028	0.0014	No Data	**280**	1,400	2,800	No Data

Table K.1. TCVP Occupational Handler Non-Cancer Risk Estimates.											
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Inhalation Dose (mg/kg/day)**				**Inhalation MOEs (LOC is an MOE = 300)** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario.			
				No R	**PF5 R**	**PF10 R**	**EC**	**No R**	**PF5 R**	**PF10 R**	**EC**
	Recreational Parks, Footpaths and Roadways										
	Beef Cattle - Direct Applied	0.026 lb ai/animal	400 animals	0.0045	0.00090	0.00045	No Data	870	4,400	8,700	No Data
	Swine - Direct Applied	0.049 lb ai/animal		0.0085	0.0017	0.00085	No Data	460	2,300	4,600	No Data
	Lactating Dairy Cattle - Direct Applied	0.0049 lb ai/animal		0.00085	0.00017	0.000085	No Data	4,600	23,000	46,000	No Data
		0.0013 lb ai/animal		0.00023	0.00045	0.000023	No Data	17,000	87,000	170,000	No Data
	Poultry Buildings (Walls, Ceilings, Floors, Larvicide) -	0.00077 lb ai/sq ft	20,000 sq ft	0.0067	0.0013	0.00067	No Data	590	2,900	5,900	No Data
	Poultry Buildings (Floor Management, Fowl Tick, Larvicide)	0.00064 lb ai/sq ft		0.0056	0.0011	0.00056	No Data	710	3,500	7,100	No Data
	Poultry (Caged) - Direct Applied	0.00032 lb ai/bird	20,000 birds	0.0028	0.00054	0.00027	No Data	1,400	7,100	14,000	No Data
	Poultry Buildings (Flies Residual) -	0.00013 lb ai/sq ft	20,000 sq ft	0.0011	0.00023	0.00011	No Data	3,500	17,000	35,000	No Data
	Poultry (Chicken on Litter) - Direct Applied	0.000078 lb ai/bird	20,000 birds	0.00068	0.00014	0.000068	No Data	5,800	29,000	58,000	No Data
	Poultry Floor Management	0.000064 lb ai/sq ft	20,000 sq ft	0.00056	0.00011	0.000056	No Data	7,100	35,000	71,000	No Data
(9c) Liquid: Mechanically -Pressurized Handgun	Beef Cattle - Direct Applied	0.039 lb ai/animal	400 animals	0.018	0.0036	0.0018	No Data	**220**	1,100	2,200	No Data
		0.032 lb ai/animal		0.015	0.0029	0.0015	No Data	**270**	1,300	2,700	No Data
	Woody Borders of Kennels, Yards, Campgrounds, Recreational Parks,	0.026 lb ai/animal		0.012	0.0024	0.0012	No Data	330	1,700	3,300	No Data

Table K.1. TCVP Occupational Handler Non-Cancer Risk Estimates.											
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Inhalation Dose (mg/kg/day)**				**Inhalation MOEs (LOC is an MOE = 300)** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario.			
				No R	**PF5 R**	**PF10 R**	**EC**	**No R**	**PF5 R**	**PF10 R**	**EC**
	Footpaths and Roadways										
	Beef Cattle - Direct Applied	0.049 lb ai/animal		0.023	0.0045	0.0023	No Data	**180**	880	1,800	No Data
	Swine - Direct Applied	0.0049 lb ai/animal		0.0023	0.00045	0.00023	No Data	1,800	8,800	18,000	No Data
	Lactating Dairy Cattle - Direct Applied	0.0013 lb ai/animal		0.00060	0.00012	0.000060	No Data	6,600	33,000	66,000	No Data
	Poultry Buildings (Walls, Ceilings, Floors, Larvicide) -	0.00077 lb ai/sq ft	20,000 sq ft	0.018	0.0035	0.0018	No Data	**220**	1,100	2,200	No Data
	Poultry Buildings (Floor Management, Fowl Tick, Larvicide)	0.00064 lb ai/sq ft		0.015	0.0029	0.0015	No Data	**270**	1,300	2,700	No Data
	Poultry (Caged) - Direct Applied	0.00032 lb ai/bird	20,000 birds	0.0073	0.0015	0.00073	No Data	540	2,700	5,400	No Data
	Poultry Buildings (Flies Residual)	0.00013 lb ai/sq ft	20,000 sq ft	0.0030	0.00060	0.00023	No Data	1,300	6,600	13,000	No Data
	Poultry (Chicken on Litter) - Direct Applied	0.000078 lb ai/bird	20,000 birds	0.0018	0.00036	0.00018	No Data	2,200	11,000	22,000	No Data
	Poultry Floor Management	0.000064 lb ai/sq ft	20,000 sq ft	0.0015	0.00029	0.00015	No Data	2,700	13,000	27,000	No Data
(9d) Liquid: Backrubber or Facerubber	Cattle - Direct Applied	0.077 lb ai/gallon	50 (gallons/ day)	1.2E-05	2.5E-06	1.2E-06	No Data	320,000	1,600,000	3,200,000	No Data
		0.064 lb ai/gallon		1.0E-05	2.0E-06	1.0E-06	No Data	390,000	1,900,000	3,900,000	No Data
(10a) Wettable Powder: Backpack Sprayer	Beef Cattle - Direct Spray	0.040 lb ai/animal	400 animals	0.0070	0.0014	0.00070	No Data	570	2,800	5,700	No Data
	Swine - Direct Spray	0.020 lb ai/animal		0.0035	0.00070	0.00035	No Data	1,100	5,700	11,000	No Data
	Poultry (Floor Management Litter,	0.00080 lb ai/sq ft	20,000 sq ft	0.0070	0.0014	0.00070	No Data	570	2,800	5,700	No Data

Table K.1. TCVP Occupational Handler Non-Cancer Risk Estimates.											
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Inhalation Dose (mg/kg/day)**				**Inhalation MOEs (LOC is an MOE = 300)** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario.			
				No R	**PF5 R**	**PF10 R**	**EC**	**No R**	**PF5 R**	**PF10 R**	**EC**
	Fowl Tick), Poultry Droppings, Manure Piles, Garbage Piles, Under Feed Troughs										
	Poultry (Wire Cages) - Direct Spray	0.00040 lb ai/bird	20,000 birds	0.0035	0.00070	0.00035	No Data	1,100	5,700	11,000	No Data
	Dairy Barns, Poultry Houses, Swine Barns, or other Animal Buildings	0.00032 lb ai/sq ft	20,000 sq ft	0.0028	0.00056	0.00028	No Data	1,400	7,100	14,000	No Data
	Dairy Barns, Poultry Houses, Swine Barns, or other Animal Buildings	0.00016 lb ai/sq ft		0.0014	0.00028	0.00014	No Data	2,800	14,000	28,000	No Data
	Dairy Barns, Poultry Houses, Swine Barns, or other Animal Buildings	0.000080 lb ai/sq ft		0.00070	0.00014	0.000070	No Data	5,700	28,000	57,000	No Data
	Kennels, Yards, Campgrounds, Picnic Areas, and Recreational Parks	0.000040 lb ai/sq ft	1,000 sq ft (spot)	0.000017	0.0000035	0.0000017	No Data	230,000	1,100,000	2,300,000	No Data
(10b) Wettable Powder: Manually-Pressurized Handwand	Beef Cattle - Direct Spray	0.040 lb ai/animal	400 animals	0.0070	0.0014	0.00070	No Data	570	2,800	5,700	No Data
	Swine - Direct Spray	0.020 lb ai/animal		0.0035	0.00070	0.00035	No Data	1,100	5,700	11,000	No Data
	Poultry (Floor Management Litter, Fowl Tick), Poultry Droppings, Manure	0.00080 lb ai/sq ft	20,000 sq ft	0.0070	0.0014	0.00070	No Data	570	2,800	5,700	No Data

Table K.1. TCVP Occupational Handler Non-Cancer Risk Estimates.											
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Inhalation Dose (mg/kg/day)**				**Inhalation MOEs (LOC is an MOE = 300)** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario.			
				No R	**PF5 R**	**PF10 R**	**EC**	**No R**	**PF5 R**	**PF10 R**	**EC**
	Piles, Garbage Piles, Under Feed Troughs										
	Poultry (Wire Cages) - Direct Spray	0.00040 lb ai/bird	20,000 birds	0.0035	0.00070	0.00035	No Data	1,100	5,700	11,000	No Data
	Dairy Barns, Poultry Houses, Swine Barns, or other Animal Buildings	0.00032 lb ai/sq ft	20,000 sq ft	0.0028	0.00056	0.00028	No Data	1,400	7,100	14,000	No Data
		0.00016 lb ai/sq ft		0.0014	0.00028	0.00014	No Data	2,800	14,000	28,000	No Data
		0.000080 lb ai/sq ft		0.00070	0.00014	0.000070	No Data	5,700	28,000	57,000	No Data
	Kennels, Yards, Campgrounds, Picnic Areas, and Recreational Parks	0.000040 lb ai/sq ft	1,000 sq ft (spot)	0.000017	0.0000035	0.0000017	No Data	230,000	1,100,000	2,300,000	No Data
(10d) Wettable Powder: Fogging Equipment (handheld, portable, and stationary)	Poultry (Floor Management)	0.0016 lb ai/bird	20,000 birds	4.13	0.828	0.413	No Data	**1**	**5**	**10**	No Data
		0.00078 lb ai/sq ft	100,000 sq ft	10.10	2.010	1.010	No Data	**0**	**2**	**4**	No Data
	Poultry (Floor Management Litter)	0.00023 lb ai/sq ft		2.97	0.594	0.297	No Data	**1**	**7**	**13**	No Data
(10e) Wettable Powder: Rotary Duster (Dust - Plunger Data as Surrogate)	Poultry (Floor Management Litter)	0.00023 lb ai/sq ft	20,000 sq ft	0.11	0.023	0.011	No Data	**35**	**180**	350	No Data
(10f) Wettable Powder: Plunger	Poultry (Floor Management)	0.0016 lb ai/bird	1,000 birds	0.039	0.0078	0.0039	No Data	**100**	500	1,000	No Data
		0.00078 lb ai/sq ft	1,000 sq ft	0.019	0.0038	0.0019	No Data	**210**	1,000	2,100	No Data

Table K.1. TCVP Occupational Handler Non-Cancer Risk Estimates.												
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Inhalation Dose (mg/kg/day)**				**Inhalation MOEs (LOC is an MOE = 300)** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario.			
				No R	**PF5 R**	**PF10 R**	**EC**	**No R**	**PF5 R**	**PF10 R**	**EC**
Duster (Dust Data as Surrogate)	Poultry (Floor Management Litter)	0.00023 lb ai/sq ft		0.0056	0.0011	0.00056	No Data	700	3,500	7,000	No Data
(11a) Dust: Self-Treating Dust Bag	Cattle	0.75 lb ai/dust bag	10 dust bags	0.18	0.037	0.018	No Data	**21**	**110**	**210**	No Data
		0.38 lb ai/dust bag		0.093	0.019	0.0093	No Data	**42**	**210**	420	No Data
		0.13 lb ai/dust bag		0.032	0.0064	0.0032	No Data	**120**	620	1,200	No Data
(11b) Dust: Shaker Can	Cattle, Swine – Direct Applied	0.0075 lb ai/animal	400 animals	0.76	0.15	0.076	No Data	**5**	**26**	**52**	No Data
		0.0038 lb ai/animal		0.39	0.077	0.039	No Data	**10**	**51**	**100**	No Data
	Cattle – Direct Applied	0.0013 lb ai/animal		0.13	0.026	0.013	No Data	**30**	**150**	300	No Data
	Poultry (Dust Box) – Direct Applied	0.00060 lb ai/ bird	1,000 birds	0.15	0.030	0.015	No Data	**26**	**130**	**260**	No Data
	Poultry (Floor Management)	0.00030 lb ai/sq ft	1,000 sq ft	0.076	0.015	0.0076	No Data	**52**	**260**	520	No Data
	Swine - Bedding	0.00020 lb ai/sq ft		0.051	0.010	0.0051	No Data	**78**	390	780	No Data
	Poultry (Wire Cage) – Direct Applied	0.00010 lb ai/ bird	1,000 birds	0.025	0.0051	0.0025	No Data	**160**	780	1,600	No Data
(11c) Dust: Rotary Duster (Plunger Data as Surrogate)	Cattle, Swine – Direct Applied	0.0075 lb ai/animal	400 animals	0.074	0.015	0.0074	No Data	**54**	**270**	540	No Data
		0.0038 lb ai/animal		0.037	0.0075	0.0037	No Data	**110**	530	1,100	No Data
	Cattle – Direct Applied	0.0013 lb ai/animal		0.013	0.0026	0.0013	No Data	310	1,500	3,100	No Data
	Poultry (Dust Box) – Direct Applied	0.00060 lb ai/bird	20,000 birds	0.29	0.060	0.029	No Data	**13**	**67**	**130**	No Data

Table K.1. TCVP Occupational Handler Non-Cancer Risk Estimates.											
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Inhalation Dose (mg/kg/day)**				**Inhalation MOEs (LOC is an MOE = 300)** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario.			
				No R	**PF5 R**	**PF10 R**	**EC**	**No R**	**PF5 R**	**PF10 R**	**EC**
	Poultry (Floor Management)	0.00030 lb ai/sq ft	20,000 sq ft	0.15	0.029	0.015	No Data	**27**	**130**	**270**	No Data
	Poultry (Wire Cage) – Direct Applied	0.00010 lb ai/bird	20,000 birds	0.049	0.0098	0.0049	No Data	**80**	400	800	No Data
(11d) Dust: Plunger Duster	Poultry (Dust Box) – Direct Applied	0.00060 lb ai/bird	1,000 birds	0.015	0.0029	0.0015	No Data	**270**	1,300	2,700	No Data
	Poultry (Floor Management)	0.00030 lb ai/ sq ft	1,000 sq ft	0.0074	0.0015	0.00074	No Data	540	2,700	5,400	No Data
	Poultry (Wire Cage) – Direct Applied	0.00010 lb ai/bird	1,000 birds	0.0025	0.00049	0.00025	No Data	1,600	8,000	16,000	No Data
(12a) Paint: Brush or Roller	Poultry (Roost Paint)	0.08 lb ai/gallon	2 gallons	0.00065	0.00013	0.000065	No Data	6,100	30,000	61,000	No Data
		0.077 lb ai/gallon		0.00063	0.00013	0.000063	No Data	6,300	32,000	63,000	No Data
		0.064 lb ai/gallon		0.00052	0.00010	0.000052	No Data	7,600	38,000	76,000	No Data
		0.03 lb ai/gallon		0.00024	0.000049	0.000024	No Data	16,000	81,000	160,000	No Data
(12b) Paint: Airless	Poultry (Roost Paint)	0.08 lb ai/gallon	2 gallons	0.0013	0.00026	0.00013	No Data	3,000	15,000	30,000	No Data
		0.077 lb ai/gallon		0.0013	0.00025	0.00013	No Data	3,200	16,000	32,000	No Data
		0.064 lb ai/gallon		0.0010	0.00021	0.00010	No Data	3,800	19,000	38,000	No Data
		0.03 lb ai/gallon		0.00049	0.000097	0.000049	No Data	8,100	40,000	81,000	No Data
(13) Solid Feed Additive for Feed Through Applications via Cup (Granular Data as Surrogate)	Horse Feed	0.0015 lb ai/animal	500 horses	0.00014	0.000027	0.000014	No Data	29,000	140,000	290,000	No Data
		0.00077 lb ai/animal		0.000070	0.000014	0.0000070	No Data	57,000	280,000	570,000	No Data
	Cattle Feed	0.0022 lb ai/animal	1,000 cows	0.00040	0.000080	0.000040	No Data	9,900	49,000	99,000	No Data
		0.0017 lb ai/animal		0.00031	0.000062	0.000031	No Data	13,000	64,000	130,000	No Data

Table K.2. TCVP Occupational Handler Non-Cancer Risk Estimates.											
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Inhalation Dose (mg/kg/day)**				**Inhalation MOEs (LOC is an MOE = 300)** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario.			
				No R	**PF5 R**	**PF10 R**	**EC**	**No R**	**PF5 R**	**PF10 R**	**EC**
Mixer/Loaders											
(10c) Wettable Powder: Mechanically -Pressurized Handgun MRID 42622301	Beef Cattle - Direct Spray	0.040 lb ai/animal	400 animals	0.0070	No Data	No Data	No Data	570	No Data	No Data	No Data
	Swine - Direct Spray	0.020 lb ai/animal		0.0035	No Data	No Data	No Data	1,100	No Data	No Data	No Data
	Poultry (Floor Management Litter, Fowl Tick), Poultry Droppings, Manure Piles, Garbage Piles, Under Feed Troughs	0.00080 lb ai/ sq ft	100,000 sq ft	0.035	No Data	No Data	No Data	**110**	No Data	No Data	No Data
	Poultry (Wire Cages) - Direct Spray	0.00040 lb ai/birds	20,000 birds	0.0035	No Data	No Data	No Data	1,100	No Data	No Data	No Data
	Dairy Barns, Poultry Houses, Swine Barns, or other Animal Buildings	0.00032 lb ai/sq ft	100,000 sq ft	0.014	No Data	No Data	No Data	**280**	No Data	No Data	No Data
		0.00016 lb ai/sq ft		0.0070	No Data	No Data	No Data	570	No Data	No Data	No Data
		0.000080 lb ai/sq ft		0.0035	No Data	No Data	No Data	1,100	No Data	No Data	No Data
Applicators											
(10c) Wettable Powder: Mechanically -Pressurized Handgun MRID 42622301	Beef Cattle - Direct Spray	0.040 lb ai/animal	400 animals	0.0016	No Data	No Data	No Data	2,400	No Data	No Data	No Data
	Swine - Direct Spray	0.020 lb ai/animal		0.00081	No Data	No Data	No Data	4,900	No Data	No Data	No Data
	Poultry (Floor Management Litter, Fowl Tick), Poultry Droppings, Manure Piles, Garbage Piles, Under Feed Troughs	0.00080 lb ai/sq ft	100,000 sq ft	0.0081	No Data	No Data	No Data	490	No Data	No Data	No Data

Table K.2. TCVP Occupational Handler Non-Cancer Risk Estimates.											
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Inhalation Dose (mg/kg/day)**				**Inhalation MOEs (LOC is an MOE = 300)** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario.			
				No R	**PF5 R**	**PF10 R**	**EC**	**No R**	**PF5 R**	**PF10 R**	**EC**
	Poultry (Wire Cages) - Direct Spray	0.00040 lb ai/birds	20,000 birds	0.00081	No Data	No Data	No Data	4,900	No Data	No Data	No Data
	Dairy Barns, Poultry Houses, Swine Barns, or other Animal Buildings	0.00032 lb ai/sq ft	100,000 sq ft	0.0033	No Data	No Data	No Data	1,200	No Data	No Data	No Data
		0.00016 lb ai/sq ft		0.0016	No Data	No Data	No Data	2,400	No Data	No Data	No Data
		0.000080 lb ai/sq ft		0.000812	No Data	No Data	No Data	4,900	No Data	No Data	No Data
Mixer/Loader/Applicators											
(10c) Wettable Powder: Mechanically -Pressurized Handgun PHED	Beef Cattle - Direct Spray	0.040 lb ai/animal	400 animals	0.018	0.0037	0.0018	No Data	**220**	1,100	2,200	No Data
	Swine - Direct Spray	0.020 lb ai/animal		0.0092	0.0018	0.00092	No Data	430	2,200	4,300	No Data
	Poultry (Floor Management Litter, Fowl Tick), Poultry Droppings, Manure Piles, Garbage Piles, Under Feed Troughs	0.00080 lb ai/sq ft	100,000 sq ft	0.092	0.018	0.0092	No Data	**43**	**220**	430	No Data
	Poultry (Wire Cages) - Direct Spray	0.00040 lb ai/birds	20,000 birds	0.0092	0.0018	0.00092	No Data	430	2,200	4,300	No Data
	Dairy Barns, Poultry Houses, Swine Barns, or other Animal Buildings	0.00032 lb ai/sq ft	100,000 sq ft	0.037	0.0073	0.0037	No Data	**110**	540	1,100	No Data
		0.00016 lb ai/sq ft		0.018	0.0037	0.0018	No Data	**220**	1,100	2,200	No Data
		0.000080 lb ai/sq ft		0.0092	0.0018	0.00092	No Data	430	2,200	4,300	No Data

Appendix L. Summary of Occupational Handler Cancer Risk Estimates

Table L.1. TCVP Occupational Handler Cancer Risk Estimates – Private/ Farmer													
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Private/Farmer** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
Mixer/Loaders													
(1a) Mixing/ Loading Liquids for Groundboom Applications	Poultry Buildings (Including: Ceilings, Floors, Larvicide, Walls)	0.00077 lb ai/sq ft	100,000 sq ft	5E-07	9E-08	7E-08	5E-07	9E-08	7E-08	5E-07	9E-08	7E-08	2E-08
	Poultry Buildings (Including: Floor Management, Fowl Tick, Larvicide)	0.00064 lb ai/sq ft		4E-07	8E-08	6E-08	4E-07	8E-08	6E-08	4E-07	7E-08	6E-08	2E-08
	Poultry Buildings (Flies Residual)	0.00013 lb ai/sq ft		9E-08	2E-08	1E-08	9E-08	2E-08	1E-08	9E-08	2E-08	1E-08	4E-09
	Poultry Floor Management	0.000064 lb ai/sq ft		4E-08	8E-09	6E-09	4E-08	8E-09	6E-09	4E-08	7E-09	6E-09	2E-09
(1b) Mixing/ Loading Liquids for Paint Applications	Poultry Buildings (Roost)	0.077 lb ai/gallon	2 gallons	1E-09	2E-10	1E-10	1E-09	2E-10	1E-10	1E-09	2E-10	1E-10	5E-11
		0.064 lb ai/gallon		9E-10	2E-10	1E-10	9E-10	2E-10	1E-10	9E-10	1E-10	1E-10	4E-11
(2a) Mixing/ Loading Wettable Powders for Groundboom Applications	Poultry Buildings (Including: Droppings, Floor Management Litter, Fowl Tick, Garbage Piles, Manure Piles, Under Feed Troughs)	0.00080 lb ai/sq ft	100,000 sq ft	1E-05	2E-06	1E-06	9E-06	6E-07	5E-07	9E-06	5E-07	4E-07	3E-08
	Dairy Barns, Poultry Houses, Swine Barns, or Other Animal Buildings	0.00032 lb ai/ sq ft		4E-06	6E-07	6E-07	4E-06	3E-07	2E-07	4E-06	2E-07	2E-07	1E-08
(2b) Mixing/ Loading Wettable Powders for	Poultry (Floor Management – Roost)	0.080 lb ai/gallon	2 gallons	8E-09	1E-09	1E-09	7E-09	5E-10	4E-10	7E-09	4E-10	3E-10	2E-11

Table L.1. TCVP Occupational Handler Cancer Risk Estimates – Private/ Farmer												
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Private/Farmer** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
Paint Applications													
(3a) Mixing/ Loading Dusts for Paint Applications (WP Data as Surrogate)		0.030 lb ai/gallon		8E-09	1E-09	1E-09	7E-09	5E-10	4E-10	7E-09	4E-10	3E-10	2E-11
Applicators													
(4) Groundboom Applications	Poultry Buildings (Including: Droppings, Floor Management Litter, Fowl Tick, Garbage Piles, Manure Piles, Under Feed Troughs)	0.00080 lb ai/sq ft	100,000 sq ft	2E-07	5E-08	4E-08	2E-07	4E-08	3E-08	2E-07	4E-08	3E-08	1E-08
	Poultry Buildings (Including: Ceilings, Floors, Larvicide, Walls)	0.00077 lb ai/sq ft		2E-07	5E-08	4E-08	2E-07	4E-08	3E-08	2E-07	4E-08	3E-08	1E-08
	Poultry Buildings (Including: Floor Management, Fowl Tick, Larvicide)	0.00064 lb ai/sq ft		2E-07	4E-08	3E-08	2E-07	3E-08	3E-08	2E-07	3E-08	3E-08	1E-08
	Dairy Barns, Poultry Houses, Swine Barns, or Other Animal Buildings	0.00032 lb ai/sq ft		8E-08	2E-08	2E-08	8E-08	2E-08	1E-08	8E-08	2E-08	1E-08	5E-09
	Poultry Buildings (Flies Residual)	0.00013 lb ai/sq ft		3E-08	8E-09	6E-09	3E-08	7E-09	5E-09	3E-08	7E-09	5E-09	2E-09
	Poultry (Floor Management)	0.000064 lb ai/sq ft		2E-08	4E-09	3E-09	2E-08	3E-09	3E-09	2E-08	3E-09	3E-09	1E-09
	Cattle Feed	0.0039	1,000	3E-08	5E-09	4E-09	3E-08	5E-09	4E-09	3E-08	5E-09	3E-09	No Data

Table L.1. TCVP Occupational Handler Cancer Risk Estimates – Private/ Farmer													
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Private/Farmer** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
(5) Open Pour Liquid Additive for Feed Through Applications	(Concentrate)	lb ai/animal	cows										
	Cattle Feed (Concentrate)	0.0022 lb ai/animal		2E-08	3E-09	2E-09	1E-08	3E-09	2E-09	1E-08	3E-09	2E-09	No Data
	Horse Feed	0.0017 lb ai/animal	500 horses	6E-09	1E-09	8E-10	6E-09	1E-09	8E-10	6E-09	1E-09	8E-10	No Data
	Swine Feed	0.00060 lb ai/animal	6,250 pigs	3E-08	5E-09	4E-09	3E-08	4E-09	3E-09	3E-08	4E-09	3E-09	No Data
(6a) RTU Pet Collar Applications – 1/99 Liquid/Dust Ratio	Cat (2596-49)	0.0036 lb ai/animal	8 animals	4E-06	3E-07	2E-07	4E-06	1E-07	1E-07	4E-06	1E-07	8E-08	No Data
	Dog (2596-50,62) - Small	0.0061 lb ai/animal		6E-06	4E-07	4E-07	6E-06	2E-07	2E-07	6E-06	2E-07	1E-07	No Data
	Dog (2596-50,62) - Large	0.010 lb ai/animal		1E-05	7E-07	6E-07	1E-05	4E-07	3E-07	1E-05	3E-07	2E-07	No Data
	Cat (2596-63) - Small	0.0048 lb ai/animal		5E-06	3E-07	3E-07	5E-06	2E-07	1E-07	5E-06	2E-07	1E-07	No Data
	Cat (2596-63) - Large	0.0055 lb ai/animal		6E-06	4E-07	3E-07	5E-06	2E-07	1E-07	5E-06	2E-07	1E-07	No Data
	Cat (2596-83) - Small	0.0039 lb ai/animal		4E-06	3E-07	2E-07	4E-06	1E-07	1E-07	4E-06	1E-07	9E-08	No Data
	Cat (2596-83) - Large	0.0080 lb ai/animal		8E-06	6E-07	5E-07	8E-06	3E-07	2E-07	8E-06	3E-07	2E-07	No Data
	Dog (2596-84) – Small	0.0061 lb ai/animal		6E-06	4E-07	4E-07	6E-06	2E-07	2E-07	6E-06	2E-07	1E-07	No Data
	Dog (2596-84) – Large	0.010 lb ai/animal		1E-05	7E-07	6E-07	1E-05	4E-07	3E-07	1E-05	3E-07	2E-07	No Data
	Cat (2596-139) - All	0.0032 lb ai/animal		3E-06	2E-07	2E-07	3E-06	1E-07	9E-08	3E-06	1E-07	7E-08	No Data
	Dog (2596-139) - All	0.016 lb ai/animal		2E-05	1E-06	1E-06	2E-05	6E-07	4E-07	2E-05	5E-07	4E-07	No Data
	Dog (11556-164) - All	0.0072 lb ai/animal		7E-06	5E-07	4E-07	7E-06	3E-07	2E-07	7E-06	2E-07	2E-07	No Data
	Cat (11556-165) - All	0.0045 lb ai/animal		5E-06	3E-07	3E-07	4E-06	2E-07	1E-07	4E-06	1E-07	1E-07	No Data
(6b) RTU Pet Collar	Cat (2596-49)	0.0036 lb ai/animal		2E-06	2E-07	1E-07	2E-06	1E-07	7E-08	2E-06	9E-08	6E-08	No Data

Table L.1. TCVP Occupational Handler Cancer Risk Estimates – Private/ Farmer													
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Private/Farmer** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
Applications – 50/50 Liquid/Dust Ratio	Dog (2596-50,62) - Small	0.0061 lb ai/animal		3E-06	3E-07	2E-07	3E-06	2E-07	1E-07	3E-06	1E-07	1E-07	No Data
	Dog (2596-50,62) - Large	0.010 lb ai/animal		5E-06	4E-07	4E-07	5E-06	3E-07	2E-07	5E-06	2E-07	2E-07	No Data
	Cat (2596-63) - Small	0.0048 lb ai/animal		3E-06	2E-07	2E-07	2E-06	1E-07	9E-08	2E-06	1E-07	8E-08	No Data
	Cat (2596-63) - Large	0.0055 lb ai/animal		3E-06	2E-07	2E-07	3E-06	1E-07	1E-07	3E-06	1E-07	9E-08	No Data
	Cat (2596-83) - Small	0.0039 lb ai/animal		2E-06	2E-07	1E-07	2E-06	1E-07	7E-08	2E-06	9E-08	6E-08	No Data
	Cat (2596-83) - Large	0.0080 lb ai/animal		4E-06	4E-07	3E-07	4E-06	2E-07	1E-07	4E-06	2E-07	1E-07	No Data
	Dog (2596-84) – Small	0.0061 lb ai/animal		3E-06	3E-07	2E-07	3E-06	2E-07	1E-07	3E-06	1E-07	1E-07	No Data
	Dog (2596-84) – Large	0.010 lb ai/animal		5E-06	4E-07	4E-07	5E-06	3E-07	2E-07	5E-06	2E-07	2E-07	No Data
	Cat (2596-139) - All	0.0032 lb ai/animal		2E-06	1E-07	1E-07	2E-06	8E-08	6E-08	2E-06	8E-08	5E-08	No Data
	Dog (2596-139) - All	0.016 lb ai/animal		9E-06	7E-07	6E-07	8E-06	4E-07	3E-07	8E-06	4E-07	3E-07	No Data
	Dog (11556-164) - All	0.0072 lb ai/animal		4E-06	3E-07	3E-07	4E-06	2E-07	1E-07	4E-06	2E-07	1E-07	No Data
	Cat (11556-165) - All	0.0045 lb ai/animal		2E-06	2E-07	2E-07	2E-06	1E-07	8E-08	2E-06	1E-07	7E-08	No Data
(6c) RTU Pet Collar Applications – 99/1 Liquid/Dust Ratio	Cat (2596-49)	0.0036 lb ai/animal		1E-07	6E-08	4E-08	1E-07	6E-08	4E-08	1E-07	6E-08	4E-08	No Data
	Dog (2596-50,62) - Small	0.0061 lb ai/animal		2E-07	1E-07	7E-08	2E-07	1E-07	6E-08	2E-07	1E-07	6E-08	No Data
	Dog (2596-50,62) - Large	0.010 lb ai/animal		4E-07	2E-07	1E-07	4E-07	2E-07	1E-07	4E-07	2E-07	1E-07	No Data
	Cat (2596-63) - Small	0.0048 lb ai/animal		2E-07	8E-08	5E-08	2E-07	8E-08	5E-08	2E-07	8E-08	5E-08	No Data
	Cat (2596-63) - Large	0.0055 lb ai/animal		2E-07	9E-08	6E-08	2E-07	9E-08	6E-08	2E-07	9E-08	6E-08	No Data

Table L.1. TCVP Occupational Handler Cancer Risk Estimates – Private/ Farmer													
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Private/Farmer** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
	Cat (2596-83) - Small	0.0039 lb ai/animal		1E-07	7E-08	4E-08	1E-07	7E-08	4E-08	1E-07	7E-08	4E-08	No Data
	Cat (2596-83) - Large	0.0080 lb ai/animal		3E-07	1E-07	9E-08	3E-07	1E-07	8E-08	3E-07	1E-07	8E-08	No Data
	Dog (2596-84) – Small	0.0061 lb ai/animal		2E-07	1E-07	7E-08	2E-07	1E-07	6E-08	2E-07	1E-07	6E-08	No Data
	Dog (2596-84) – Large	0.010 lb ai/animal		4E-07	2E-07	1E-07	4E-07	2E-07	1E-07	4E-07	2E-07	1E-07	No Data
	Cat (2596-139) - All	0.0032 lb ai/animal		1E-07	6E-08	3E-08	1E-07	5E-08	3E-08	1E-07	5E-08	3E-08	No Data
	Dog (2596-139) - All	0.016 lb ai/animal		6E-07	3E-07	2E-07	6E-07	3E-07	2E-07	6E-07	3E-07	2E-07	No Data
	Dog (11556-164) - All	0.0072 lb ai/animal		3E-07	1E-07	8E-08	3E-07	1E-07	8E-08	3E-07	1E-07	8E-08	No Data
	Cat (11556-165) - All	0.0045 lb ai/animal		2E-07	8E-08	5E-08	2E-07	8E-08	5E-08	2E-07	8E-08	5E-08	No Data
(7) RTU Dust/Powder Applications	Dog (47000-123) - Small	0.00037 lb ai/animal		4E-07	3E-08	2E-08	4E-07	1E-08	1E-08	4E-07	1E-08	8E-09	No Data
	Dog (47000-123) - Medium	0.00094 lb ai/animal		1E-06	7E-08	6E-08	9E-07	3E-08	3E-08	9E-07	3E-08	2E-08	No Data
	Dog (47000-123) - Large	0.0015 lb ai/animal		2E-06	1E-07	9E-08	2E-06	5E-08	4E-08	2E-06	5E-08	3E-08	No Data
	Cat (47000-123) - Small	0.000090 lb ai/animal		9E-08	6E-09	6E-09	9E-08	3E-09	2E-09	9E-08	3E-09	2E-09	No Data
	Cat (47000-123) - Medium	0.00022 lb ai/animal		2E-07	2E-08	1E-08	2E-07	8E-09	6E-09	2E-07	7E-09	5E-09	No Data
	Cat (47000-123) - Large	0.00034 lb ai/animal		4E-07	2E-08	2E-08	3E-07	1E-08	9E-09	3E-07	1E-08	8E-09	No Data
	Cat (2596-78) - Small	0.00062 lb ai/animal		6E-07	4E-08	4E-08	6E-07	2E-08	2E-08	6E-07	2E-08	1E-08	No Data
	Cat (2596-78) - Large	0.0010 lb ai/animal		1E-06	7E-08	6E-08	1E-06	4E-08	3E-08	1E-06	3E-08	2E-08	No Data
	Dog (2596-79) - Small	0.0010 lb ai/animal		1E-06	7E-08	6E-08	1E-06	4E-08	3E-08	1E-06	3E-08	2E-08	No Data

Table L.1. TCVP Occupational Handler Cancer Risk Estimates – Private/ Farmer												
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Private/Farmer** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
	Dog (2596-79) - Medium	0.0021 lb ai/animal		2E-06	2E-07	1E-07	2E-06	8E-08	6E-08	2E-06	7E-08	5E-08	No Data
	Dog (2596-79) - Large	0.0026 lb ai/animal		3E-06	2E-07	2E-07	3E-06	9E-08	7E-08	3E-06	8E-08	6E-08	No Data
	Dog (67517-82) - Small	0.0011 lb ai/animal		1E-06	8E-08	7E-08	1E-06	4E-08	3E-08	1E-06	3E-08	2E-08	No Data
	Dog (67517-82) - Medium	0.0028 lb ai/animal		3E-06	2E-07	2E-07	3E-06	1E-07	8E-08	3E-06	9E-08	6E-08	No Data
	Dog (67517-82) - Large	0.0045 lb ai/animal		5E-06	3E-07	3E-07	5E-06	2E-07	1E-07	5E-06	1E-07	1E-07	No Data
	Cat (67517-82) - Small	0.00028 lb ai/animal		3E-07	2E-08	2E-08	3E-07	1E-08	8E-09	3E-07	9E-09	6E-09	No Data
	Cat (67517-82) - Medium	0.00067 lb ai/animal		7E-07	5E-08	4E-08	7E-07	2E-08	2E-08	7E-07	2E-08	2E-08	No Data
	Cat (67517-82) - Large	0.0010 lb ai/animal		1E-06	7E-08	6E-08	1E-06	4E-08	3E-08	1E-06	3E-08	2E-08	No Data
(8) RTU Pump/Trigger Spray Applications	Cat (2596-126,140) - Trigger -Small	0.00055 lb ai/animal		8E-08	7E-08	4E-08	7E-08	7E-08	4E-08	7E-08	7E-08	4E-08	No Data
	Cat (2596-126,140) - Trigger - Large	0.00077 lb ai/animal		1E-07	1E-07	6E-08	1E-07	1E-07	5E-08	1E-07	1E-07	5E-08	No Data
	Cat (2596-140) - Pump - Small	0.00011 lb ai/animal		2E-08	1E-08	8E-09	1E-08	1E-08	8E-09	1E-08	1E-08	7E-09	No Data
	Cat (2596-140) - Pump - Large	0.00016 lb ai/animal		2E-08	2E-08	1E-08	2E-08	2E-08	1E-08	2E-08	2E-08	1E-08	No Data
	Dog (2596-125,-140) - Small	0.00077 lb ai/animal		1E-07	1E-07	6E-08	1E-07	1E-07	5E-08	1E-07	1E-07	5E-08	No Data
	Dog (2596-125,-140) - Medium	0.00088 lb ai/animal		1E-07	1E-07	7E-08	1E-07	1E-07	6E-08	1E-07	1E-07	6E-08	No Data
	Dog (2596-125,-140) - Large	0.0015 lb ai/animal		2E-07	2E-07	1E-07	2E-07	2E-07	1E-07	2E-07	2E-07	1E-07	No Data
Mixers/Loaders/Applicators													
(9a) Liquid: Backpack Sprayer	Beef Cattle - Direct Applied	0.039 lb ai/animal	400 animals	4E-06	4E-06	2E-06	4E-06	4E-06	2E-06	4E-06	4E-06	2E-06	No Data
		0.032 lb ai/animal		1E-06	1E-06	8E-07	1E-06	1E-06	7E-07	1E-06	1E-06	6E-07	No Data

Table L.1. TCVP Occupational Handler Cancer Risk Estimates – Private/ Farmer												
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Private/Farmer** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
	Woody Borders of Kennels, Yards, Campgrounds, Recreational Parks, Footpaths and Roadways	0.032 lb ai/sq ft	1,000 sq ft (spot)	3E-06	3E-06	2E-06	3E-06	3E-06	2E-06	3E-06	2E-06	2E-06	No Data
	Beef Cattle - Direct Applied	0.026 lb ai/animal	400 animals	9E-07	9E-07	6E-07	8E-07	8E-07	5E-07	8E-07	8E-07	5E-07	No Data
	Swine - Direct Applied	0.049 lb ai/animal		2E-06	2E-06	1E-06	2E-06	2E-06	1E-06	2E-06	2E-06	1E-06	No Data
	Lactating Dairy Cattle - Direct Applied	0.0049 lb ai/animal		2E-07	2E-07	1E-07	2E-07	2E-07	1E-07	2E-07	2E-07	1E-07	No Data
		0.0013 lb ai/animal		5E-08	5E-08	3E-08	4E-08	4E-08	3E-08	4E-08	4E-08	3E-08	No Data
	Poultry Buildings (Walls, Ceilings, Floors, Larvicide)	0.00077 lb ai/sq ft	20,000 sq ft	1E-06	1E-06	9E-07	1E-06	1E-06	8E-07	1E-06	1E-06	8E-07	No Data
	Poultry Buildings (Floor Management, Fowl Tick, Larvicide)	0.00064 lb ai/sq ft		1E-06	1E-06	8E-07	1E-06	1E-06	7E-07	1E-06	1E-06	6E-07	No Data
	Poultry (Caged) - Direct Applied	0.00032 lb ai/bird	20,000 birds	6E-07	6E-07	4E-07	5E-07	5E-07	3E-07	5E-07	5E-07	3E-07	No Data
	Poultry Buildings (Flies Residual) -	0.00013 lb ai/sq ft	20,000 sq ft	2E-07	2E-07	2E-07	2E-07	2E-07	1E-07	2E-07	2E-07	1E-07	No Data
	Poultry (Chicken on Litter) - Direct Applied	0.000078 lb ai/bird	20,000 birds	1E-07	1E-07	9E-08	1E-07	1E-07	8E-08	1E-07	1E-07	8E-08	No Data
	Poultry Floor Management	0.000064 lb ai/sq ft	20,000 sq ft	1E-07	1E-07	8E-08	1E-07	1E-07	7E-08	1E-07	1E-07	6E-08	No Data
(9b) Liquid: Manually-Pressurized Handwand	Beef Cattle - Direct Applied	0.039 lb ai/animal	400 animals	5E-05	4E-07	3E-07	5E-05	2E-07	2E-07	5E-05	2E-07	2E-07	No Data
		0.032 lb ai/animal		4E-05	3E-07	3E-07	4E-05	2E-07	2E-07	4E-05	2E-07	2E-07	No Data

Table L.1. TCVP Occupational Handler Cancer Risk Estimates – Private/ Farmer												
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Private/Farmer** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
	Woody Borders of Kennels, Yards, Campgrounds, Recreational Parks, Footpaths and Roadways	0.032 lb ai/sq ft	1,000 sq ft (spot)	1E-04	7E-07	7E-07	1E-04	5E-07	4E-07	1E-04	5E-07	4E-07	No Data
	Beef Cattle - Direct Applied	0.026 lb ai/animal	400 animals	3E-05	2E-07	2E-07	3E-05	2E-07	1E-07	3E-05	1E-07	1E-07	No Data
	Swine - Direct Applied	0.049 lb ai/animal		6E-05	4E-07	4E-07	6E-05	3E-07	3E-07	6E-05	3E-07	2E-07	No Data
	Lactating Dairy Cattle - Direct Applied	0.0049 lb ai/animal		6E-06	4E-08	4E-08	6E-06	3E-08	3E-08	6E-06	3E-08	2E-08	No Data
		0.0013 lb ai/animal		2E-06	1E-08	1E-08	2E-06	8E-09	7E-09	2E-06	7E-09	6E-09	No Data
	Poultry Buildings (Walls, Ceilings, Floors, Larvicide) -	0.00077 lb ai/sq ft	20,000 sq ft	5E-05	4E-07	3E-07	5E-05	2E-07	2E-07	5E-05	2E-07	2E-07	No Data
	Poultry Buildings (Floor Management, Fowl Tick, Larvicide)	0.00064 lb ai/sq ft		4E-05	3E-07	3E-07	4E-05	2E-07	2E-07	4E-05	2E-07	2E-07	No Data
	Poultry (Caged) - Direct Applied	0.00032 lb ai/bird	20,000 birds	2E-05	1E-07	1E-07	2E-05	1E-07	8E-08	2E-05	9E-08	8E-08	No Data
	Poultry Buildings (Flies Residual) -	0.00013 lb ai/sq ft	20,000 sq ft	8E-06	6E-08	5E-08	8E-06	4E-08	3E-08	8E-06	4E-08	3E-08	No Data
	Poultry (Chicken on Litter) - Direct Applied	0.000078 lb ai/bird	20,000 birds	5E-06	4E-08	3E-08	5E-06	2E-08	2E-08	5E-06	2E-08	2E-08	No Data
	Poultry Floor Management	0.000064 lb ai/sq ft	20,000 sq ft	4E-06	3E-08	3E-08	4E-06	2E-08	2E-08	4E-06	2E-08	2E-08	No Data
(9c) Liquid: Mechanically -Pressurized Handgun	Beef Cattle - Direct Applied	0.039 lb ai/animal	400 animals	1E-06	7E-07	6E-07	9E-07	4E-07	3E-07	9E-07	3E-07	2E-07	No Data
		0.032 lb ai/animal		1E-06	6E-07	5E-07	8E-07	3E-07	2E-07	7E-07	3E-07	2E-07	No Data

Table L.1. TCVP Occupational Handler Cancer Risk Estimates – Private/ Farmer												
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Private/Farmer** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
	Woody Borders of Kennels, Yards, Campgrounds, Recreational Parks, Footpaths and Roadways	0.026 lb ai/animal		8E-07	5E-07	4E-07	6E-07	3E-07	2E-07	6E-07	2E-07	1E-07	No Data
	Beef Cattle - Direct Applied	0.049 lb ai/animal		2E-06	9E-07	7E-07	1E-06	5E-07	3E-07	1E-06	4E-07	3E-07	No Data
	Swine - Direct Applied	0.0049 lb ai/animal		2E-07	9E-08	7E-08	1E-07	5E-08	3E-08	1E-07	4E-08	3E-08	No Data
	Lactating Dairy Cattle - Direct Applied	0.0013 lb ai/animal		4E-08	2E-08	2E-08	3E-08	1E-08	8E-09	3E-08	1E-08	7E-09	No Data
	Poultry Buildings (Walls, Ceilings, Floors, Larvicide) -	0.00077 lb ai/sq ft	20,000 sq ft	1E-06	7E-07	6E-07	9E-07	4E-07	3E-07	9E-07	3E-07	2E-07	No Data
	Poultry Buildings (Floor Management, Fowl Tick, Larvicide)	0.00064 lb ai/sq ft		1E-06	6E-07	5E-07	8E-07	3E-07	2E-07	7E-07	3E-07	2E-07	No Data
	Poultry (Caged) - Direct Applied	0.00032 lb ai/bird	20,000 birds	5E-07	3E-07	2E-07	4E-07	2E-07	1E-07	4E-07	1E-07	9E-08	No Data
	Poultry Buildings (Flies Residual)	0.00013 lb ai/sq ft	20,000 sq ft	2E-07	1E-07	9E-08	2E-07	6E-08	4E-08	2E-07	6E-08	4E-08	No Data
	Poultry (Chicken on Litter) - Direct Applied	0.000078 lb ai/bird	20,000 birds	1E-07	7E-08	6E-08	9E-08	4E-08	3E-08	9E-08	3E-08	2E-08	No Data
	Poultry Floor Management	0.000064 lb ai/sq ft	20,000 sq ft	1E-07	6E-08	5E-08	8E-08	3E-08	2E-08	7E-08	3E-08	2E-08	No Data
(9d) Liquid: Backrubber or Facerubber	Cattle - Direct Applied	0.077 lb ai/gallon	50 (gallons/ day)	3E-08	5E-09	4E-09	3E-08	5E-09	3E-09	3E-08	5E-09	3E-09	No Data
		0.064 lb ai/gallon		2E-08	4E-09	3E-09	2E-08	4E-09	3E-09	2E-08	4E-09	3E-09	No Data
(10a) Wettable	Beef Cattle - Direct Spray	0.040 lb ai/animal	400 animals	1E-06	1E-06	9E-07	1E-06	1E-06	8E-07	1E-06	1E-06	8E-07	No Data

Table L.1. TCVP Occupational Handler Cancer Risk Estimates – Private/ Farmer												
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Private/Farmer** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
Powder: Backpack Sprayer	Swine - Direct Spray	0.020 lb ai/animal		7E-07	7E-07	5E-07	6E-07	6E-07	4E-07	6E-07	6E-07	4E-07	No Data
	Poultry (Floor Management Litter, Fowl Tick), Poultry Droppings, Manure Piles, Garbage Piles, Under Feed Troughs	0.00080 lb ai/sq ft	20,000 sq ft	1E-06	1E-06	9E-07	1E-06	1E-06	8E-07	1E-06	1E-06	8E-07	No Data
	Poultry (Wire Cages) - Direct Spray	0.00040 lb ai/bird	20,000 birds	7E-07	7E-07	5E-07	6E-07	6E-07	4E-07	6E-07	6E-07	4E-07	No Data
	Dairy Barns, Poultry Houses, Swine Barns, or other Animal Buildings	0.00032 lb ai/ sq ft	20,000 sq ft	6E-07	6E-07	4E-07	5E-07	5E-07	3E-07	5E-07	5E-07	3E-07	No Data
	Dairy Barns, Poultry Houses, Swine Barns, or other Animal Buildings	0.00016 lb ai/sq ft		3E-07	3E-07	2E-07	3E-07	3E-07	2E-07	3E-07	2E-07	2E-07	No Data
	Dairy Barns, Poultry Houses, Swine Barns, or other Animal Buildings	0.000080 lb ai/sq ft		1E-07	1E-07	9E-08	1E-07	1E-07	8E-08	1E-07	1E-07	8E-08	No Data
	Kennels, Yards, Campgrounds, Picnic Areas, and Recreational Parks	0.000040 lb ai/sq ft	1,000 sq ft (spot)	3E-09	3E-09	2E-09	3E-09	3E-09	2E-09	3E-09	3E-09	2E-09	No Data
(10b) Wettable Powder: Manually-Pressurized Handwand	Beef Cattle - Direct Spray	0.040 lb ai/animal	400 animals	5E-05	4E-07	3E-07	5E-05	2E-07	2E-07	5E-05	2E-07	2E-07	No Data
	Swine - Direct Spray	0.020 lb ai/animal		2E-05	2E-07	2E-07	2E-05	1E-07	1E-07	2E-05	1E-07	1E-07	No Data
	Poultry (Floor Management Litter,	0.00080 lb ai/sq ft	20,000 sq ft	5E-05	4E-07	3E-07	5E-05	2E-07	2E-07	5E-05	2E-07	2E-07	No Data

Table L.1. TCVP Occupational Handler Cancer Risk Estimates – Private/ Farmer													
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Private/Farmer** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
	Fowl Tick), Poultry Droppings, Manure Piles, Garbage Piles, Under Feed Troughs												
	Poultry (Wire Cages) - Direct Spray	0.00040 lb ai/bird	20,000 birds	2E-05	2E-07	2E-07	2E-05	1E-07	1E-07	2E-05	1E-07	1E-07	No Data
	Dairy Barns, Poultry Houses, Swine Barns, or other Animal Buildings	0.00032 lb ai/sq ft	20,000 sq ft	2E-05	1E-07	1E-07	2E-05	1E-07	8E-08	2E-05	9E-08	8E-08	No Data
		0.00016 lb ai/sq ft		1E-05	7E-08	7E-08	1E-05	5E-08	4E-08	1E-05	5E-08	4E-08	No Data
		0.000080 lb ai/sq ft		5E-06	4E-08	3E-08	5E-06	2E-08	2E-08	5E-06	2E-08	2E-08	No Data
	Kennels, Yards, Campgrounds, Picnic Areas, and Recreational Parks	0.000040 lb ai/sq ft	1,000 sq ft (spot)	1E-07	9E-10	8E-10	1E-07	6E-10	5E-10	1E-07	6E-10	5E-10	No Data
(10d) Wettable Powder: Fogging Equipment (handheld, portable, and stationary)	Poultry (Floor Management)	0.0016 lb ai/bird	20,000 birds	9E-05	9E-05	9E-05	2E-05	2E-05	2E-05	9E-06	9E-06	9E-06	No Data
		0.00078 lb ai/sq ft	100,000 sq ft	2E-04	2E-04	2E-04	4E-05	4E-05	4E-05	2E-05	2E-05	2E-05	No Data
	Poultry (Floor Management Litter)	0.00023 lb ai/sq ft		7E-05	7E-05	7E-05	1E-05	1E-05	1E-05	7E-06	7E-06	7E-06	No Data
(10e) Wettable Powder: Rotary Duster (Dust - Plunger Data as Surrogate)	Poultry (Floor Management Litter)	0.00023 lb ai/sq ft	20,000 sq ft	6E-04	9E-05	7E-05	6E-04	8E-05	7E-05	6E-04	8E-05	7E-05	No Data
(10f) Wettable Powder: Plunger	Poultry (Floor Management)	0.0016 lb ai/bird	1,000 birds	9E-06	2E-06	2E-06	8E-06	1E-06	1E-06	8E-06	1E-06	1E-06	No Data
		0.00078 lb ai/sq ft	1,000 sq ft	4E-06	1E-06	9E-07	4E-06	7E-07	6E-07	4E-06	6E-07	5E-07	No Data

Table L.1. TCVP Occupational Handler Cancer Risk Estimates – Private/ Farmer													
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Private/Farmer** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
Duster (Dust Data as Surrogate)	Poultry (Floor Management Litter)	0.00023 lb ai/sq ft		1E-06	3E-07	3E-07	1E-06	2E-07	2E-07	1E-06	2E-07	2E-07	No Data
(11a) Dust: Self-Treating Dust Bag	Cattle	0.75 lb ai/dust bag	10 dust bags	4E-05	1E-05	9E-06	4E-05	7E-06	6E-06	4E-05	6E-06	5E-06	No Data
		0.38 lb ai/dust bag		2E-05	5E-06	4E-06	2E-05	3E-06	3E-06	2E-05	3E-06	3E-06	No Data
		0.13 lb ai/dust bag		7E-06	2E-06	2E-06	7E-06	1E-06	1E-06	7E-06	1E-06	9E-07	No Data
(11b) Dust: Shaker Can	Cattle, Swine – Direct Applied	0.0075 lb ai/animal	400 animals	4E-04	3E-05	2E-05	4E-04	1E-05	1E-05	4E-04	1E-05	8E-06	No Data
		0.0038 lb ai/animal		2E-04	1E-05	1E-05	2E-04	7E-06	5E-06	2E-04	6E-06	4E-06	No Data
	Cattle – Direct Applied	0.0013 lb ai/animal		7E-05	5E-06	4E-06	7E-05	2E-06	2E-06	6E-05	2E-06	1E-06	No Data
	Poultry (Dust Box) – Direct Applied	0.00060 lb ai/bird	1,000 birds	8E-05	5E-06	5E-06	8E-05	3E-06	2E-06	8E-05	2E-06	2E-06	No Data
	Poultry (Floor Management)	0.00030 lb ai/sq ft	1,000 sq ft	4E-05	3E-06	2E-06	4E-05	1E-06	1E-06	4E-05	1E-06	8E-07	No Data
	Swine - Bedding	0.00020 lb ai/sq ft		3E-05	2E-06	2E-06	3E-05	9E-07	7E-07	3E-05	8E-07	6E-07	No Data
	Poultry (Wire Cage) – Direct Applied	0.00010 lb ai/bird	1,000 birds	1E-05	9E-07	8E-07	1E-05	5E-07	3E-07	1E-05	4E-07	3E-07	No Data
(11c) Dust: Rotary Duster (Plunger Data as Surrogate)	Cattle, Swine – Direct Applied	0.0075 lb ai/animal	400 animals	6E-04	9E-05	7E-05	6E-04	8E-05	7E-05	6E-04	8E-05	7E-05	No Data
		0.0038 lb ai/animal		6E-04	9E-05	7E-05	6E-04	8E-05	7E-05	6E-04	8E-05	7E-05	No Data
	Cattle – Direct Applied	0.0013 lb ai/animal		6E-04	9E-05	7E-05	6E-04	8E-05	7E-05	6E-04	8E-05	7E-05	No Data
	Poultry (Dust Box) – Direct Applied	0.00060 lb ai/bird	20,000 birds	6E-04	9E-05	7E-05	6E-04	8E-05	7E-05	6E-04	8E-05	7E-05	No Data

Table L.1. TCVP Occupational Handler Cancer Risk Estimates – Private/ Farmer													
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Private/Farmer** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
	Poultry (Floor Management)	0.00030 lb ai/sq ft	20,000 sq ft	6E-04	9E-05	7E-05	6E-04	8E-05	7E-05	6E-04	8E-05	7E-05	No Data
	Poultry (Wire Cage) – Direct Applied	0.00010 lb ai/bird	20,000 birds	6E-04	9E-05	7E-05	6E-04	8E-05	7E-05	6E-04	8E-05	7E-05	No Data
(11d) Dust: Plunger Duster	Poultry (Dust Box) – Direct Applied	0.00060 lb ai/bird	1,000 birds	6E-04	9E-05	7E-05	6E-04	8E-05	7E-05	6E-04	8E-05	7E-05	No Data
	Poultry (Floor Management)	0.00030 lb ai/sq ft	1,000 sq ft	1E-05	2E-06	1E-06	1E-05	2E-06	1E-06	1E-05	2E-06	1E-06	No Data
	Poultry (Wire Cage) – Direct Applied	0.00010 lb ai/bird	1,000 birds	3E-04	4E-05	4E-05	3E-04	4E-05	3E-05	3E-04	4E-05	3E-05	No Data
(12a) Paint: Brush or Roller	Poultry (Roost Paint)	0.08 lb ai/gallon	2 gallons	9E-07	1E-07	1E-07	9E-07	1E-07	1E-07	9E-07	1E-07	1E-07	No Data
		0.077 lb ai/gallon		9E-07	1E-07	1E-07	9E-07	1E-07	1E-07	9E-07	1E-07	1E-07	No Data
		0.064 lb ai/gallon		7E-08	1E-08	1E-08	7E-08	1E-08	9E-09	7E-08	1E-08	9E-09	No Data
		0.03 lb ai/gallon		3E-07	5E-08	5E-08	3E-07	5E-08	4E-08	3E-07	4E-08	4E-08	No Data
(12b) Paint: Airless	Poultry (Roost Paint)	0.08 lb ai/gallon	2 gallons	2E-07	9E-08	8E-08	2E-07	6E-08	6E-08	2E-07	6E-08	6E-08	No Data
		0.077 lb ai/gallon		2E-07	8E-08	8E-08	2E-07	6E-08	6E-08	2E-07	6E-08	5E-08	No Data
		0.064 lb ai/gallon		2E-08	7E-09	6E-09	2E-08	5E-09	5E-09	2E-08	5E-09	4E-09	No Data
		0.03 lb ai/gallon		9E-08	3E-08	3E-08	8E-08	2E-08	2E-08	8E-08	2E-08	2E-08	No Data
(13) Solid Feed Additive for Feed Through Applications via Cup (Granular Data as Surrogate)	Horse Feed	0.0015 lb ai/animal	500 horses	1E-09	7E-10	7E-10	6E-10	2E-10	2E-10	6E-10	1E-10	1E-10	No Data
		0.00077 lb ai/animal		6E-10	3E-10	3E-10	3E-10	9E-11	9E-11	3E-10	6E-11	6E-11	No Data
	Cattle Feed	0.0022 lb ai/animal	1,000 cows	2E-08	1E-08	1E-08	9E-09	3E-09	3E-09	8E-09	2E-09	2E-09	No Data
		0.0017 lb ai/animal		1E-08	7E-09	7E-09	7E-09	2E-09	2E-09	7E-09	1E-09	1E-09	No Data

Table L.2. TCVP Occupational Handler Cancer Risk Estimates for Exposure Scenario 10c with Use of Chemical-Specific Data and PHED – Private/Farmer													
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Private/Farmer** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
Mixer/Loaders													
(10c) Wettable Powder: Mechanically -Pressurized Handgun MRID 42622301	Beef Cattle - Direct Spray	0.040 lb ai/animal	400 animals	No Data	3E-07	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
	Swine - Direct Spray	0.020 lb ai/animal		No Data	2E-07	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
	Poultry (Floor Management Litter, Fowl Tick), Poultry Droppings, Manure Piles, Garbage Piles, Under Feed Troughs	0.00080 lb ai/sq ft	20,000 sq ft	No Data	2E-06	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
	Poultry (Wire Cages) - Direct Spray	0.00040 lb ai/bird	20,000 birds	No Data	2E-07	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
	Dairy Barns, Poultry Houses, Swine Barns, or other Animal Buildings	0.00032 lb ai/sq ft	20,000 sq ft	No Data	7E-07	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
		0.00016 lb ai/sq ft		No Data	3E-07	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
		0.000080 lb ai/sq ft		No Data	2E-07	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
Applicators													
(10c) Wettable Powder: Mechanically -Pressurized Handgun MRID 42622301	Beef Cattle - Direct Spray	0.040 lb ai/animal	400 animals	No Data	5E-07	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
	Swine - Direct Spray	0.020 lb ai/animal		No Data	2E-07	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
	Poultry (Floor Management Litter, Fowl Tick), Poultry Droppings, Manure Piles, Garbage Piles, Under Feed Troughs	0.00080 lb ai/sq ft	20,000 sq ft	No Data	2E-06	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
	Poultry (Wire Cages) - Direct Spray	0.00040	20,000 birds	No Data	2E-07	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
		0.00032	20,000	No Data	1E-06	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data

Table L.2. TCVP Occupational Handler Cancer Risk Estimates for Exposure Scenario 10c with Use of Chemical-Specific Data and PHED – Private/Farmer													
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Private/Farmer** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
	Dairy Barns, Poultry Houses, Swine Barns, or other Animal Buildings	lb ai/sq ft	sq ft										
		0.00016 lb ai/sq ft		No Data	5E-07	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
		0.000080 lb ai/sq ft		No Data	2E-07	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
Mixer/Loader/Applicators													
(10c) Wettable Powder: Mechanically -Pressurized Handgun PHED	Beef Cattle - Direct Spray	0.040 lb ai/animal	400 animals	1E-06	7E-07	6E-07	1E-06	4E-07	3E-07	9E-07	4E-07	2E-07	No Data
	Swine - Direct Spray	0.020 lb ai/animal		6E-07	4E-07	3E-07	5E-07	2E-07	1E-07	5E-07	2E-07	1E-07	No Data
	Poultry (Floor Management Litter, Fowl Tick), Poultry Droppings, Manure Piles, Garbage Piles, Under Feed Troughs	0.00080 lb ai/sq ft	20,000 sq ft	6E-06	4E-06	3E-06	5E-06	2E-06	1E-06	5E-06	2E-06	1E-06	No Data
	Poultry (Wire Cages) - Direct Spray	0.00040	20,000 birds	6E-07	4E-07	3E-07	5E-07	2E-07	1E-07	5E-07	2E-07	1E-07	No Data
	Dairy Barns, Poultry Houses, Swine Barns, or other Animal Buildings	0.00032 lb ai/sq ft	20,000 sq ft	3E-06	1E-06	1E-06	2E-06	8E-07	5E-07	2E-06	7E-07	4E-07	No Data
		0.00016 lb ai/sq ft		1E-06	7E-07	6E-07	1E-06	4E-07	3E-07	9E-07	4E-07	2E-07	No Data
		0.000080 lb ai/sq ft		6E-07	4E-07	3E-07	5E-07	2E-07	1E-07	5E-07	2E-07	1E-07	No Data

Table L.3. TCVP Occupational Handler Cancer Risk Estimates – Contract/ Commercial													
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Contract/ Commercial** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
Mixer/Loaders													
(1a) Mixing/ Loading Liquids for Groundboom Applications	Poultry Buildings (Including: Ceilings, Floors, Larvicide, Walls)	0.00077 lb ai/sq ft	100,000 (sq ft/day)	2E-06	3E-07	2E-07	2E-06	3E-07	2E-07	2E-06	3E-07	2E-07	7E-08
	Poultry Buildings (Including: Floor Management, Fowl Tick, Larvicide)	0.00064 lb ai/sq ft		1E-06	2E-07	2E-07	1E-06	2E-07	2E-07	1E-06	2E-07	2E-07	6E-08
	Poultry Buildings (Flies Residual)	0.00013 lb ai/sq ft		3E-07	5E-08	4E-08	3E-07	5E-08	4E-08	3E-07	5E-08	4E-08	1E-08
	Poultry Floor Management	0.000064 lb ai/sq ft		1E-07	2E-08	2E-08	1E-07	2E-08	2E-08	1E-07	2E-08	2E-08	6E-09
(1b) Mixing/ Loading Liquids for Paint Applications	Poultry Buildings (Roost)	0.077 lb ai/gallon	2 gallons	3E-09	6E-10	4E-10	3E-09	5E-10	4E-10	3E-09	5E-10	4E-10	1E-10
		0.064 lb ai/gallon		3E-09	5E-10	4E-10	3E-09	5E-10	3E-10	3E-09	4E-10	3E-10	1E-10
(2a) Mixing/ Loading Wettable Powders for Groundboom Applications	Poultry Buildings (Including: Droppings, Floor Management Litter, Fowl Tick, Garbage Piles, Manure Piles, Under Feed Troughs)	0.00080 lb ai/sq ft	100,000 sq ft	3E-05	5E-06	4E-06	3E-05	2E-06	2E-06	3E-05	2E-06	1E-06	9E-08
	Dairy Barns, Poultry Houses, Swine Barns, or Other Animal Buildings	0.00032 lb ai/sq ft		1E-05	2E-06	2E-06	1E-05	8E-07	7E-07	1E-05	6E-07	5E-07	4E-08
(2b) Mixing/ Loading		0.080 lb ai/gallon	2 gallons	2E-08	3E-09	3E-09	2E-08	1E-09	1E-09	2E-08	1E-09	1E-09	7E-11

Table L.3. TCVP Occupational Handler Cancer Risk Estimates – Contract/ Commercial													
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Contract/ Commercial** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
Wettable Powders for Paint Applications	Poultry (Floor Management – Roost)												
(3a) Mixing/ Loading Dusts for Paint Applications (WP Data as Surrogate)		0.030 lb ai/gallon		2E-08	3E-09	3E-09	2E-08	1E-09	1E-09	2E-08	1E-09	1E-09	7E-11
Applicators													
(4) Groundboom Applications	Poultry Buildings (Including: Droppings, Floor Management Litter, Fowl Tick, Garbage Piles, Manure Piles, Under Feed Troughs)	0.00080 lb ai/sq ft	100,000 sq ft	6E-07	1E-07	1E-07	6E-07	1E-07	1E-07	6E-07	1E-07	1E-07	4E-08
	Poultry Buildings (Including: Ceilings, Floors, Larvicide, Walls)	0.00077 lb ai/sq ft		6E-07	1E-07	1E-07	6E-07	1E-07	9E-08	6E-07	1E-07	9E-08	4E-08
	Poultry Buildings (Including: Floor Management, Fowl Tick, Larvicide)	0.00064 lb ai/sq ft		5E-07	1E-07	1E-07	5E-07	1E-07	8E-08	5E-07	1E-07	8E-08	3E-08
	Dairy Barns, Poultry Houses, Swine Barns, or Other Animal Buildings	0.00032 lb ai/sq ft		2E-07	6E-08	5E-08	2E-07	5E-08	4E-08	2E-07	5E-08	4E-08	2E-08
	Poultry Buildings (Flies Residual)	0.00013 lb ai/sq ft		1E-07	2E-08	2E-08	9E-08	2E-08	2E-08	9E-08	2E-08	2E-08	7E-09

Table L.3. TCVP Occupational Handler Cancer Risk Estimates – Contract/ Commercial													
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Contract/ Commercial** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
	Poultry (Floor Management)	0.000064 lb ai/sq ft		5E-08	1E-08	1E-08	5E-08	1E-08	8E-09	5E-08	1E-08	8E-09	3E-09
(5) Open Pour Liquid Additive for Feed Through Applications	Cattle Feed (Concentrate)	0.0039 lb ai/animal	1,000 cows	8E-08	1E-08	1E-08	8E-08	1E-08	1E-08	8E-08	1E-08	1E-08	No Data
	Cattle Feed (Concentrate)	0.0022 lb ai/animal		5E-08	8E-09	6E-09	4E-08	8E-09	6E-09	4E-08	8E-09	6E-09	No Data
	Horse Feed	0.0017 lb ai/animal	500 horses	2E-08	3E-09	2E-09	2E-08	3E-09	2E-09	2E-08	3E-09	2E-09	No Data
	Swine Feed	0.00060 lb ai/animal	6,250 pigs	8E-08	1E-08	1E-08	8E-08	1E-08	1E-08	8E-08	1E-08	1E-08	No Data
(6a) RTU Pet Collar Applications – 1/99 Liquid/Dust Ratio	Cat (2596-49)	0.0036 lb ai/animal	8 animals	1E-05	8E-07	7E-07	1E-05	4E-07	3E-07	1E-05	3E-07	2E-07	No Data
	Dog (2596-50,62) - Small	0.0061 lb ai/animal		2E-05	1E-06	1E-06	2E-05	7E-07	5E-07	2E-05	6E-07	4E-07	No Data
	Dog (2596-50,62) - Large	0.010 lb ai/animal		3E-05	2E-06	2E-06	3E-05	1E-06	8E-07	3E-05	9E-07	7E-07	No Data
	Cat (2596-63) - Small	0.0048 lb ai/animal		1E-05	1E-06	9E-07	1E-05	5E-07	4E-07	1E-05	5E-07	3E-07	No Data
	Cat (2596-63) - Large	0.0055 lb ai/animal		2E-05	1E-06	1E-06	2E-05	6E-07	4E-07	2E-05	5E-07	4E-07	No Data
	Cat (2596-83) - Small	0.0039 lb ai/animal		1E-05	8E-07	7E-07	1E-05	4E-07	3E-07	1E-05	4E-07	3E-07	No Data
	Cat (2596-83) - Large	0.0080 lb ai/animal		2E-05	2E-06	1E-06	2E-05	9E-07	6E-07	2E-05	8E-07	5E-07	No Data
	Dog (2596-84) – Small	0.0061 lb ai/animal		2E-05	1E-06	1E-06	2E-05	7E-07	5E-07	2E-05	6E-07	4E-07	No Data
	Dog (2596-84) – Large	0.010 lb ai/animal		3E-05	2E-06	2E-06	3E-05	1E-06	8E-07	3E-05	9E-07	7E-07	No Data
	Cat (2596-139) - All	0.0032 lb ai/animal		1E-05	7E-07	6E-07	9E-06	3E-07	3E-07	9E-06	3E-07	2E-07	No Data
	Dog (2596-139) - All	0.016 lb ai/animal		5E-05	3E-06	3E-06	5E-05	2E-06	1E-06	5E-05	2E-06	1E-06	No Data
	Dog (11556-164) - All	0.0072 lb ai/animal		2E-05	2E-06	1E-06	2E-05	8E-07	6E-07	2E-05	7E-07	5E-07	No Data

Table L.3. TCVP Occupational Handler Cancer Risk Estimates – Contract/ Commercial													
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Contract/ Commercial** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/NoG PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
	Cat (11556-165) - All	0.0045 lb ai/animal		1E-05	1E-06	8E-07	1E-05	5E-07	4E-07	1E-05	4E-07	3E-07	No Data
(6b) RTU Pet Collar Applications - 50/50 Liquid/Dust Ratio	Cat (2596-49)	0.0036 lb ai/animal		6E-06	5E-07	4E-07	6E-06	3E-07	2E-07	6E-06	3E-07	2E-07	No Data
	Dog (2596-50,62) - Small	0.0061 lb ai/animal		1E-05	8E-07	7E-07	9E-06	5E-07	3E-07	9E-06	4E-07	3E-07	No Data
	Dog (2596-50,62) - Large	0.010 lb ai/animal		2E-05	1E-06	1E-06	2E-05	8E-07	6E-07	2E-05	7E-07	5E-07	No Data
	Cat (2596-63) - Small	0.0048 lb ai/animal		8E-06	6E-07	5E-07	7E-06	4E-07	3E-07	7E-06	3E-07	2E-07	No Data
	Cat (2596-63) - Large	0.0055 lb ai/animal		9E-06	7E-07	6E-07	9E-06	4E-07	3E-07	8E-06	4E-07	3E-07	No Data
	Cat (2596-83) - Small	0.0039 lb ai/animal		6E-06	5E-07	4E-07	6E-06	3E-07	2E-07	6E-06	3E-07	2E-07	No Data
	Cat (2596-83) - Large	0.0080 lb ai/animal		1E-05	1E-06	9E-07	1E-05	6E-07	4E-07	1E-05	6E-07	4E-07	No Data
	Dog (2596-84) – Small	0.0061 lb ai/animal		1E-05	8E-07	7E-07	9E-06	5E-07	3E-07	9E-06	4E-07	3E-07	No Data
	Dog (2596-84) – Large	0.010 lb ai/animal		2E-05	1E-06	1E-06	2E-05	8E-07	6E-07	2E-05	7E-07	5E-07	No Data
	Cat (2596-139) - All	0.0032 lb ai/animal		5E-06	4E-07	4E-07	5E-06	3E-07	2E-07	5E-06	2E-07	2E-07	No Data
	Dog (2596-139) - All	0.016 lb ai/animal		3E-05	2E-06	2E-06	2E-05	1E-06	9E-07	2E-05	1E-06	8E-07	No Data
	Dog (11556-164) - All	0.0072 lb ai/animal		1E-05	1E-06	8E-07	1E-05	6E-07	4E-07	1E-05	5E-07	4E-07	No Data
	Cat (11556-165) - All	0.0045 lb ai/animal		7E-06	6E-07	5E-07	7E-06	4E-07	3E-07	7E-06	3E-07	2E-07	No Data
(6c) RTU Pet Collar Applications - 99/1 Liquid/Dust Ratio	Cat (2596-49)	0.0036 lb ai/animal		4E-07	2E-07	1E-07	4E-07	2E-07	1E-07	4E-07	2E-07	1E-07	No Data
	Dog (2596-50,62) - Small	0.0061 lb ai/animal		7E-07	3E-07	2E-07	7E-07	3E-07	2E-07	7E-07	3E-07	2E-07	No Data
	Dog (2596-50,62) - Large	0.010 lb ai/animal		1E-06	5E-07	3E-07	1E-06	5E-07	3E-07	1E-06	5E-07	3E-07	No Data

Table L.3. TCVP Occupational Handler Cancer Risk Estimates – Contract/ Commercial													
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Contract/ Commercial** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
	Cat (2596-63) - Small	0.0048 lb ai/animal		5E-07	2E-07	2E-07	5E-07	2E-07	2E-07	5E-07	2E-07	2E-07	No Data
	Cat (2596-63) - Large	0.0055 lb ai/animal		6E-07	3E-07	2E-07	6E-07	3E-07	2E-07	6E-07	3E-07	2E-07	No Data
	Cat (2596-83) - Small	0.0039 lb ai/animal		4E-07	2E-07	1E-07	4E-07	2E-07	1E-07	4E-07	2E-07	1E-07	No Data
	Cat (2596-83) - Large	0.0080 lb ai/animal		9E-07	4E-07	3E-07	9E-07	4E-07	3E-07	9E-07	4E-07	3E-07	No Data
	Dog (2596-84) – Small	0.0061 lb ai/animal		7E-07	3E-07	2E-07	7E-07	3E-07	2E-07	7E-07	3E-07	2E-07	No Data
	Dog (2596-84) – Large	0.010 lb ai/animal		1E-06	5E-07	3E-07	1E-06	5E-07	3E-07	1E-06	5E-07	3E-07	No Data
	Cat (2596-139) - All	0.0032 lb ai/animal		4E-07	2E-07	1E-07	4E-07	2E-07	1E-07	4E-07	2E-07	1E-07	No Data
	Dog (2596-139) - All	0.016 lb ai/animal		2E-06	8E-07	5E-07	2E-06	8E-07	5E-07	2E-06	8E-07	5E-07	No Data
	Dog (11556-164) - All	0.0072 lb ai/animal		8E-07	4E-07	2E-07	8E-07	4E-07	2E-07	8E-07	4E-07	2E-07	No Data
	Cat (11556-165) - All	0.0045 lb ai/animal		5E-07	2E-07	1E-07	5E-07	2E-07	1E-07	5E-07	2E-07	1E-07	No Data
(7) RTU Dust/Powder Applications	Dog (47000-123) - Small	0.00037 lb ai/animal		1E-07	1E-07	9E-08	1E-07	1E-07	8E-08	1E-07	1E-07	8E-08	No Data
	Dog (47000-123) - Medium	0.00094 lb ai/animal		4E-06	4E-06	3E-06	4E-06	4E-06	2E-06	4E-06	4E-06	2E-06	No Data
	Dog (47000-123) - Large	0.0015 lb ai/animal		3E-06	3E-06	2E-06	3E-06	3E-06	2E-06	3E-06	3E-06	2E-06	No Data
	Cat (47000-123) - Small	0.000090 lb ai/animal		2E-06	2E-06	1E-06	2E-06	2E-06	1E-06	2E-06	2E-06	1E-06	No Data
	Cat (47000-123) - Medium	0.00022 lb ai/animal		1E-05	1E-05	6E-06	1E-05	1E-05	6E-06	1E-05	1E-05	6E-06	No Data
	Cat (47000-123) - Large	0.00034 lb ai/animal		3E-06	3E-06	2E-06	3E-06	3E-06	2E-06	3E-06	3E-06	2E-06	No Data
	Cat (2596-78) - Small	0.00062 lb ai/animal		8E-06	8E-06	6E-06	8E-06	8E-06	5E-06	8E-06	7E-06	5E-06	No Data

Table L.3. TCVP Occupational Handler Cancer Risk Estimates – Contract/ Commercial													
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Contract/ Commercial** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
	Cat (2596-78) - Large	0.0010 lb ai/animal		3E-06	3E-06	2E-06	2E-06	2E-06	2E-06	2E-06	2E-06	2E-06	No Data
	Dog (2596-79) - Small	0.0010 lb ai/animal		5E-06	5E-06	3E-06	5E-06	5E-06	3E-06	5E-06	5E-06	3E-06	No Data
	Dog (2596-79) - Medium	0.0021 lb ai/animal		5E-07	5E-07	3E-07	5E-07	5E-07	3E-07	5E-07	5E-07	3E-07	No Data
	Dog (2596-79) - Large	0.0026 lb ai/animal		1E-07	1E-07	9E-08	1E-07	1E-07	8E-08	1E-07	1E-07	8E-08	No Data
	Dog (67517-82) - Small	0.0011 lb ai/animal		4E-06	4E-06	3E-06	4E-06	4E-06	2E-06	4E-06	4E-06	2E-06	No Data
	Dog (67517-82) - Medium	0.0028 lb ai/animal		3E-06	3E-06	2E-06	3E-06	3E-06	2E-06	3E-06	3E-06	2E-06	No Data
	Dog (67517-82) - Large	0.0045 lb ai/animal		2E-06	2E-06	1E-06	2E-06	2E-06	1E-06	2E-06	2E-06	1E-06	No Data
	Cat (67517-82) - Small	0.00028 lb ai/animal		1E-05	1E-05	6E-06	1E-05	1E-05	6E-06	1E-05	1E-05	6E-06	No Data
	Cat (67517-82) - Medium	0.00067 lb ai/animal		3E-06	3E-06	2E-06	3E-06	3E-06	2E-06	3E-06	3E-06	2E-06	No Data
	Cat (67517-82) - Large	0.0010 lb ai/animal		8E-06	8E-06	6E-06	8E-06	8E-06	5E-06	8E-06	7E-06	5E-06	No Data
(8) RTU Pump/Trigger Spray Applications	Cat (2596-126,140) - Trigger -Small	0.00055 lb ai/animal		3E-06	3E-06	2E-06	2E-06	2E-06	2E-06	2E-06	2E-06	2E-06	No Data
	Cat (2596-126,140) - Trigger - Large	0.00077 lb ai/animal		5E-06	5E-06	3E-06	5E-06	5E-06	3E-06	5E-06	5E-06	3E-06	No Data
	Cat (2596-140) - Pump - Small	0.00011 lb ai/animal		5E-07	5E-07	3E-07	5E-07	5E-07	3E-07	5E-07	5E-07	3E-07	No Data
	Cat (2596-140) - Pump - Large	0.00016 lb ai/animal		1E-07	1E-07	9E-08	1E-07	1E-07	8E-08	1E-07	1E-07	8E-08	No Data
	Dog (2596-125,-140) - Small	0.00077 lb ai/animal		4E-06	4E-06	3E-06	4E-06	4E-06	2E-06	4E-06	4E-06	2E-06	No Data
	Dog (2596-125,-140) - Medium	0.00088 lb ai/animal		3E-06	3E-06	2E-06	3E-06	3E-06	2E-06	3E-06	3E-06	2E-06	No Data
	Dog (2596-125,-140) - Large	0.0015 lb ai/animal		2E-06	2E-06	1E-06	2E-06	2E-06	1E-06	2E-06	2E-06	1E-06	No Data
Mixers/Loaders/Applicators													

Table L.3. TCVP Occupational Handler Cancer Risk Estimates – Contract/ Commercial													
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Contract/ Commercial** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
(9a) Liquid: Backpack Sprayer	Beef Cattle - Direct Applied	0.039 lb ai/animal	400 animals	1E-05	1E-05	6E-06	1E-05	1E-05	6E-06	1E-05	1E-05	6E-06	No Data
		0.032 lb ai/animal		3E-06	3E-06	2E-06	3E-06	3E-06	2E-06	3E-06	3E-06	2E-06	No Data
	Woody Borders of Kennels, Yards, Campgrounds, Recreational Parks, Footpaths and Roadways	0.032 lb ai/sq ft	1,000 sq ft (spot)	8E-06	8E-06	6E-06	8E-06	8E-06	5E-06	8E-06	7E-06	5E-06	No Data
	Beef Cattle - Direct Applied	0.026 lb ai/animal	400 animals	3E-06	3E-06	2E-06	2E-06	2E-06	2E-06	2E-06	2E-06	2E-06	No Data
	Swine - Direct Applied	0.049 lb ai/animal		5E-06	5E-06	3E-06	5E-06	5E-06	3E-06	5E-06	5E-06	3E-06	No Data
	Lactating Dairy Cattle - Direct Applied	0.0049 lb ai/animal		5E-07	5E-07	3E-07	5E-07	5E-07	3E-07	5E-07	5E-07	3E-07	No Data
		0.0013 lb ai/animal		1E-07	1E-07	9E-08	1E-07	1E-07	8E-08	1E-07	1E-07	8E-08	No Data
	Poultry Buildings (Walls, Ceilings, Floors, Larvicide)	0.00077 lb ai/sq ft	20,000 sq ft	4E-06	4E-06	3E-06	4E-06	4E-06	2E-06	4E-06	4E-06	2E-06	No Data
	Poultry Buildings (Floor Management, Fowl Tick, Larvicide)	0.00064 lb ai/sq ft		3E-06	3E-06	2E-06	3E-06	3E-06	2E-06	3E-06	3E-06	2E-06	No Data
	Poultry (Caged) - Direct Applied	0.00032 lb ai/bird	20,000 birds	2E-06	2E-06	1E-06	2E-06	2E-06	1E-06	2E-06	2E-06	1E-06	No Data
	Poultry Buildings (Flies Residual) -	0.00013 lb ai/sq ft	20,000 sq ft	7E-07	7E-07	5E-07	6E-07	6E-07	4E-07	6E-07	6E-07	4E-07	No Data
	Poultry (Chicken on Litter) - Direct Applied	0.000078 lb ai/bird	20,000 birds	4E-07	4E-07	3E-07	4E-07	4E-07	2E-07	4E-07	4E-07	2E-07	No Data
	Poultry Floor Management	0.000064 lb ai/sq ft	20,000 sq ft	3E-07	3E-07	2E-07	3E-07	3E-07	2E-07	3E-07	3E-07	2E-07	No Data
(9b) Liquid:		0.039	400	1E-04	1E-06	1E-06	1E-04	7E-07	6E-07	1E-04	7E-07	6E-07	No Data

Table L.3. TCVP Occupational Handler Cancer Risk Estimates – Contract/ Commercial												
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Contract/ Commercial** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
Manually-Pressurized Handwand	Beef Cattle - Direct Applied	lb ai/animal	animals										
		0.032 lb ai/animal		1E-04	9E-07	8E-07	1E-04	6E-07	5E-07	1E-04	5E-07	5E-07	No Data
	Woody Borders of Kennels, Yards, Campgrounds, Recreational Parks, Footpaths and Roadways	0.032 lb ai/sq ft	1,000 sq ft (spot)	3E-04	2E-06	2E-06	3E-04	1E-06	1E-06	3E-04	1E-06	1E-06	No Data
	Beef Cattle - Direct Applied	0.026 lb ai/animal	400 animals	1E-04	7E-07	7E-07	1E-04	5E-07	4E-07	1E-04	4E-07	4E-07	No Data
	Swine - Direct Applied	0.049 lb ai/animal		2E-04	1E-06	1E-06	2E-04	9E-07	8E-07	2E-04	8E-07	7E-07	No Data
	Lactating Dairy Cattle - Direct Applied	0.0049 lb ai/animal		2E-05	1E-07	1E-07	2E-05	9E-08	8E-08	2E-05	8E-08	7E-08	No Data
		0.0013 lb ai/animal		5E-06	4E-08	3E-08	5E-06	2E-08	2E-08	5E-06	2E-08	2E-08	No Data
	Poultry Buildings (Walls, Ceilings, Floors, Larvicide) -	0.00077 lb ai/sq ft	20,000 sq ft	1E-04	1E-06	1E-06	1E-04	7E-07	6E-07	1E-04	7E-07	6E-07	No Data
	Poultry Buildings (Floor Management, Fowl Tick, Larvicide)	0.00064 lb ai/sq ft		1E-04	9E-07	8E-07	1E-04	6E-07	5E-07	1E-04	5E-07	5E-07	No Data
	Poultry (Caged) - Direct Applied	0.00032 lb ai/bird	20,000 birds	6E-05	4E-07	4E-07	6E-05	3E-07	3E-07	6E-05	3E-07	2E-07	No Data
	Poultry Buildings (Flies Residual) -	0.00013 lb ai/sq ft	20,000 sq ft	2E-05	2E-07	2E-07	2E-05	1E-07	1E-07	2E-05	1E-07	9E-08	No Data
	Poultry (Chicken on Litter) - Direct Applied	0.000078 lb ai/bird	20,000 birds	1E-05	1E-07	1E-07	1E-05	7E-08	6E-08	1E-05	7E-08	6E-08	No Data
	Poultry Floor Management	0.000064 lb ai/sq ft	20,000 sq ft	1E-05	9E-08	8E-08	1E-05	6E-08	5E-08	1E-05	5E-08	5E-08	No Data
(9c) Liquid:	Beef Cattle - Direct Applied	0.039 lb ai/animal	400 animals	4E-06	2E-06	2E-06	3E-06	1E-06	8E-07	3E-06	1E-06	6E-07	No Data

Table L.3. TCVP Occupational Handler Cancer Risk Estimates – Contract/ Commercial												
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Contract/ Commercial** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/NoG PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
Mechanically -Pressurized Handgun		0.032 lb ai/animal		3E-06	2E-06	1E-06	2E-06	9E-07	6E-07	2E-06	9E-07	5E-07	No Data
	Woody Borders of Kennels, Yards, Campgrounds, Recreational Parks, Footpaths and Roadways	0.026 lb ai/animal		3E-06	1E-06	1E-06	2E-06	8E-07	5E-07	2E-06	7E-07	4E-07	No Data
	Beef Cattle - Direct Applied	0.049 lb ai/animal		5E-06	3E-06	2E-06	4E-06	1E-06	1E-06	3E-06	1E-06	8E-07	No Data
	Swine - Direct Applied	0.0049 lb ai/animal		5E-07	3E-07	2E-07	4E-07	1E-07	1E-07	3E-07	1E-07	8E-08	No Data
	Lactating Dairy Cattle - Direct Applied	0.0013 lb ai/animal		1E-07	7E-08	6E-08	9E-08	4E-08	3E-08	9E-08	3E-08	2E-08	No Data
	Poultry Buildings (Walls, Ceilings, Floors, Larvicide) -	0.00077 lb ai/sq ft	20,000 sq ft	4E-06	2E-06	2E-06	3E-06	1E-06	8E-07	3E-06	1E-06	6E-07	No Data
	Poultry Buildings (Floor Management, Fowl Tick, Larvicide)	0.00064 lb ai/sq ft		3E-06	2E-06	1E-06	2E-06	9E-07	6E-07	2E-06	9E-07	5E-07	No Data
	Poultry (Caged) - Direct Applied	0.00032 lb ai/bird	20,000 birds	2E-06	9E-07	7E-07	1E-06	5E-07	3E-07	1E-06	4E-07	3E-07	No Data
	Poultry Buildings (Flies Residual)	0.00013 lb ai/sq ft	20,000 sq ft	6E-07	4E-07	3E-07	5E-07	2E-07	1E-07	5E-07	2E-07	1E-07	No Data
	Poultry (Chicken on Litter) - Direct Applied	0.000078 lb ai/bird	20,000 birds	4E-07	2E-07	2E-07	3E-07	1E-07	8E-08	3E-07	1E-07	6E-08	No Data
	Poultry Floor Management	0.000064 lb ai/sq ft	20,000 sq ft	3E-07	2E-07	1E-07	2E-07	9E-08	6E-08	2E-07	9E-08	5E-08	No Data
(9d) Liquid: Backrubber or Facerubber	Cattle - Direct Applied	0.077 lb ai/gallon	50 gallons	8E-08	1E-08	1E-08	8E-08	1E-08	1E-08	8E-08	1E-08	1E-08	No Data
		0.064 lb ai/gallon		7E-08	1E-08	9E-09	7E-08	1E-08	9E-09	7E-08	1E-08	9E-09	No Data

Table L.3. TCVP Occupational Handler Cancer Risk Estimates – Contract/ Commercial													
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Contract/ Commercial** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
(10a) Wettable Powder: Backpack Sprayer	Beef Cattle - Direct Spray	0.040 lb ai/animal	400 animals	4E-06	4E-06	3E-06	4E-06	4E-06	2E-06	4E-06	4E-06	2E-06	No Data
	Swine - Direct Spray	0.020 lb ai/animal		2E-06	2E-06	1E-06	2E-06	2E-06	1E-06	2E-06	2E-06	1E-06	No Data
	Poultry (Floor Management Litter, Fowl Tick), Poultry Droppings, Manure Piles, Garbage Piles, Under Feed Troughs	0.00080 lb ai/sq ft	20,000 sq ft	4E-06	4E-06	3E-06	4E-06	4E-06	2E-06	4E-06	4E-06	2E-06	No Data
	Poultry (Wire Cages) - Direct Spray	0.00040 lb ai/bird	20,000 birds	2E-06	2E-06	1E-06	2E-06	2E-06	1E-06	2E-06	2E-06	1E-06	No Data
	Dairy Barns, Poultry Houses, Swine Barns, or other Animal Buildings	0.00032 lb ai/sq ft	20,000 sq ft	2E-06	2E-06	1E-06	2E-06	2E-06	1E-06	2E-06	2E-06	1E-06	No Data
	Dairy Barns, Poultry Houses, Swine Barns, or other Animal Buildings	0.00016 lb ai/sq ft		8E-07	8E-07	6E-07	8E-07	8E-07	5E-07	8E-07	7E-07	5E-07	No Data
	Dairy Barns, Poultry Houses, Swine Barns, or other Animal Buildings	0.000080 lb ai/sq ft		4E-07	4E-07	3E-07	4E-07	4E-07	2E-07	4E-07	4E-07	2E-07	No Data
	Kennels, Yards, Campgrounds, Picnic Areas, and Recreational Parks	0.000040 lb ai/sq ft	1,000 sq ft (spot)	1E-08	1E-08	7E-09	9E-09	9E-09	6E-09	9E-09	9E-09	6E-09	No Data
(10b) Wettable	Beef Cattle - Direct Spray	0.040 lb ai/animal	400 animals	1E-04	1E-06	1E-06	1E-04	7E-07	6E-07	1E-04	7E-07	6E-07	No Data

Table L.3. TCVP Occupational Handler Cancer Risk Estimates – Contract/ Commercial												
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Contract/ Commercial** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
Powder: Manually-Pressurized Handwand	Swine - Direct Spray	0.020 lb ai/animal		7E-05	5E-07	5E-07	7E-05	4E-07	3E-07	7E-05	3E-07	3E-07	No Data
	Poultry (Floor Management Litter, Fowl Tick), Poultry Droppings, Manure Piles, Garbage Piles, Under Feed Troughs	0.00080 lb ai/sq ft	20,000 sq ft	1E-04	1E-06	1E-06	1E-04	7E-07	6E-07	1E-04	7E-07	6E-07	No Data
	Poultry (Wire Cages) - Direct Spray	0.00040 lb ai/bird	20,000 birds	7E-05	5E-07	5E-07	7E-05	4E-07	3E-07	7E-05	3E-07	3E-07	No Data
	Dairy Barns, Poultry Houses, Swine Barns, or other Animal Buildings	0.00032 lb ai/sq ft	20,000 sq ft	6E-05	4E-07	4E-07	6E-05	3E-07	3E-07	6E-05	3E-07	2E-07	No Data
		0.00016 lb ai/sq ft		3E-05	2E-07	2E-07	3E-05	1E-07	1E-07	3E-05	1E-07	1E-07	No Data
		0.000080 lb ai/sq ft		1E-05	1E-07	1E-07	1E-05	7E-08	6E-08	1E-05	7E-08	6E-08	No Data
	Kennels, Yards, Campgrounds, Picnic Areas, and Recreational Parks	0.000040 lb ai/sq ft	1,000 sq ft (spot)	4E-07	3E-09	3E-09	4E-07	2E-09	2E-09	4E-07	2E-09	1E-09	No Data
(10d) Wettable Powder: Fogging Equipment (handheld, portable, and stationary)	Poultry (Floor Management)	0.0016 lb ai/bird	20,000 birds	3E-04	3E-04	3E-04	2E-03	2E-04	2E-04	2E-03	2E-04	2E-04	No Data
		0.00078 lb ai/sq ft	100,000 sq ft	7E-04	7E-04	7E-04	2E-03	2E-04	2E-04	2E-03	2E-04	2E-04	No Data
	Poultry (Floor Management Litter)	0.00023 lb ai/sq ft		2E-04	2E-04	2E-04	2E-03	2E-04	2E-04	2E-03	2E-04	2E-04	No Data
(10e) Wettable Powder: Rotary Duster (Dust -	Poultry (Floor Management Litter)	0.00023 lb ai/sq ft	20,000 sq ft	2E-03	3E-04	2E-04	2E-03	2E-04	2E-04	2E-03	2E-04	2E-04	No Data

Table L.3. TCVP Occupational Handler Cancer Risk Estimates – Contract/ Commercial													
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Contract/ Commercial** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
Plunger Data as Surrogate)													
(10f) Wettable Powder: Plunger Duster (Dust Data as Surrogate)	Poultry (Floor Management)	0.0016 lb ai/bird	1,000 birds	3E-05	6E-06	6E-06	3E-05	4E-06	4E-06	2E-05	4E-06	3E-06	No Data
		0.00078 lb ai/sq ft	1,000 sq ft	1E-05	3E-06	3E-06	1E-05	2E-06	2E-06	1E-05	2E-06	2E-06	No Data
	Poultry (Floor Management Litter)	0.00023 lb ai/sq ft		4E-06	9E-07	8E-07	4E-06	6E-07	5E-07	4E-06	6E-07	5E-07	No Data
(11a) Dust: Self-Treating Dust Bag	Cattle	0.75 lb ai/dust bag	10 dust bags	1E-04	3E-05	3E-05	1E-04	2E-05	2E-05	1E-04	2E-05	2E-05	No Data
		0.38 lb ai/dust bag		6E-05	1E-05	1E-05	6E-05	1E-05	9E-06	6E-05	9E-06	8E-06	No Data
		0.13 lb ai/dust bag		2E-05	5E-06	5E-06	2E-05	3E-06	3E-06	2E-05	3E-06	3E-06	No Data
(11b) Dust: Shaker Can (Plunger Data Surrogate)	Cattle, Swine – Direct Applied	0.0075 lb ai/animal	400 animals	1E-03	8E-05	7E-05	1E-03	4E-05	3E-05	1E-03	4E-05	3E-05	No Data
		0.0038 lb ai/animal		6E-04	4E-05	4E-05	6E-04	2E-05	2E-05	6E-04	2E-05	1E-05	No Data
	Cattle – Direct Applied	0.0013 lb ai/animal		2E-04	1E-05	1E-05	2E-04	7E-06	5E-06	2E-04	6E-06	4E-06	No Data
	Poultry (Dust Box) – Direct Applied	0.00060 lb ai/ bird	1,000 birds	2E-04	2E-05	1E-05	2E-04	8E-06	6E-06	2E-04	7E-06	5E-06	No Data
	Poultry (Floor Management)	0.00030 lb ai/sq ft	1,000 sq ft	1E-04	8E-06	7E-06	1E-04	4E-06	3E-06	1E-04	4E-06	3E-06	No Data
	Swine - Bedding	0.00020 lb ai/sq ft		8E-05	5E-06	5E-06	8E-05	3E-06	2E-06	8E-05	2E-06	2E-06	No Data

Table L.3. TCVP Occupational Handler Cancer Risk Estimates – Contract/ Commercial													
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Contract/ Commercial** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
	Poultry (Wire Cage) – Direct Applied	0.00010 lb ai/bird	1,000 birds	4E-05	3E-06	2E-06	4E-05	1E-06	1E-06	4E-05	1E-06	8E-07	No Data
(11c) Dust: Rotary Duster (Plunger Data as Surrogate)	Cattle, Swine – Direct Applied	0.0075 lb ai/animal	400 animals	2E-03	3E-04	2E-04	2E-03	2E-04	2E-04	2E-03	2E-04	2E-04	No Data
		0.0038 lb ai/animal		2E-03	3E-04	2E-04	2E-03	2E-04	2E-04	2E-03	2E-04	2E-04	No Data
	Cattle – Direct Applied	0.0013 lb ai/animal		2E-03	3E-04	2E-04	2E-03	2E-04	2E-04	2E-03	2E-04	2E-04	No Data
	Poultry (Dust Box) – Direct Applied	0.00060 lb ai/bird	20,000 birds	2E-03	3E-04	2E-04	2E-03	2E-04	2E-04	2E-03	2E-04	2E-04	No Data
	Poultry (Floor Management)	0.00030 lb ai/sq ft	20,000 sq ft	2E-03	3E-04	2E-04	2E-03	2E-04	2E-04	2E-03	2E-04	2E-04	No Data
	Poultry (Wire Cage) – Direct Applied	0.00010 lb ai/bird	20,000 birds	2E-03	3E-04	2E-04	2E-03	2E-04	2E-04	2E-03	2E-04	2E-04	No Data
(11d) Dust: Plunger Duster	Poultry (Dust Box) – Direct Applied	0.00060 lb ai/bird	1,000 birds	2E-03	3E-04	2E-04	2E-03	2E-04	2E-04	2E-03	2E-04	2E-04	No Data
	Poultry (Floor Management)	0.00030 lb ai/sq ft	1,000 sq ft	3E-05	5E-06	4E-06	3E-05	5E-06	4E-06	3E-05	5E-06	4E-06	No Data
	Poultry (Wire Cage) – Direct Applied	0.00010 lb ai/bird	1,000 birds	8E-04	1E-04	1E-04	8E-04	1E-04	1E-04	8E-04	1E-04	1E-04	No Data
(12a) Paint: Brush or Roller	Poultry (Roost Paint)	0.08 lb ai/gallon	2 gallons	3E-06	4E-07	4E-07	3E-06	4E-07	3E-07	3E-06	4E-07	3E-07	No Data
		0.077 lb ai/gallon		3E-06	4E-07	4E-07	3E-06	4E-07	3E-07	3E-06	3E-07	3E-07	No Data
		0.064 lb ai/gallon		2E-07	3E-08	3E-08	2E-07	3E-08	3E-08	2E-07	3E-08	3E-08	No Data
		0.03 lb ai/gallon		1E-06	1E-07	1E-07	1E-06	1E-07	1E-07	1E-06	1E-07	1E-07	No Data

Table L.3. TCVP Occupational Handler Cancer Risk Estimates – Contract/ Commercial														
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Contract/ Commercial** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
(12b) Paint: Airless	Poultry (Roost Paint)	0.08 lb ai/gallon	2 gallons	7E-07	3E-07	2E-07	6E-07	2E-07	2E-07	6E-07	2E-07	2E-07	No Data
		0.077 lb ai/gallon		7E-07	2E-07	2E-07	6E-07	2E-07	2E-07	6E-07	2E-07	2E-07	No Data
		0.064 lb ai/gallon		6E-08	2E-08	2E-08	5E-08	2E-08	1E-08	5E-08	1E-08	1E-08	No Data
		0.03 lb ai/gallon		3E-07	1E-07	9E-08	2E-07	7E-08	7E-08	2E-07	7E-08	6E-08	No Data
(13) Solid Feed Additive for Feed Through Applications via Cup (Granular Data as Surrogate)	Horse Feed	0.0015 lb ai/animal	500 horses	3E-09	2E-09	2E-09	2E-09	5E-10	5E-10	2E-09	3E-10	3E-10	No Data
		0.00077 lb ai/animal		2E-09	1E-09	1E-09	1E-09	3E-10	3E-10	9E-10	2E-10	2E-10	No Data
	Cattle Feed	0.0022 lb ai/animal	1,000 cows	5E-08	3E-08	3E-08	3E-08	8E-09	8E-09	3E-08	5E-09	5E-09	No Data
		0.0017 lb ai/animal		4E-08	2E-08	2E-08	2E-08	6E-09	6E-09	2E-08	4E-09	4E-09	No Data

Table L.4. TCVP Occupational Handler Cancer Risk Estimates for Exposure Scenario 10c with Use of Chemical-Specific Data and PHED – Contract/Commercial														
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Contract/Commercial** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario.									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
Mixer/Loaders														
(10c) Wettable Powder:	Beef Cattle - Direct Spray	0.040 lb ai/animal	400 animals	No Data	1E-06	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
	Swine - Direct Spray	0.020 lb ai/animal		No Data	5E-07	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data

Table L.4. TCVP Occupational Handler Cancer Risk Estimates for Exposure Scenario 10c with Use of Chemical-Specific Data and PHED – Contract/Commercial													
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Contract/Commercial** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario.									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
Mechanically -Pressurized Handgun MRID 42622301	Poultry (Floor Management Litter, Fowl Tick), Poultry Droppings, Manure Piles, Garbage Piles, Under Feed Troughs	0.00080 lb ai/sq ft	20,000 sq ft	No Data	5E-06	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
	Poultry (Wire Cages) - Direct Spray	0.00040 lb ai/bird	20,000 birds	No Data	5E-07	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
	Dairy Barns, Poultry Houses, Swine Barns, or other Animal Buildings	0.00032 lb ai/sq ft	20,000 sq ft	No Data	2E-06	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
		0.00016 lb ai/sq ft		No Data	1E-06	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
		0.000080 lb ai/sq ft		No Data	5E-07	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
Applicators													
(10c) Wettable Powder: Mechanically -Pressurized Handgun MRID 42622301	Beef Cattle - Direct Spray	0.040 lb ai/animal	400 animals	No Data	1E-06	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
	Swine - Direct Spray	0.020 lb ai/animal		No Data	7E-07	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
	Poultry (Floor Management Litter, Fowl Tick), Poultry Droppings, Manure Piles, Garbage Piles, Under Feed Troughs	0.00080 lb ai/sq ft	20,000 sq ft	No Data	7E-06	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
	Poultry (Wire Cages) - Direct Spray	0.00040 lb ai/bird	20,000 birds	No Data	7E-07	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
	Dairy Barns, Poultry Houses, Swine Barns, or other Animal Buildings	0.00032 lb ai/sq ft	20,000 sq ft	No Data	3E-06	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
		0.00016 lb ai/sq ft		No Data	1E-06	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
		0.000080 lb ai/sq ft		No Data	7E-07	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data

Table L.4. TCVP Occupational Handler Cancer Risk Estimates for Exposure Scenario 10c with Use of Chemical-Specific Data and PHED – Contract/Commercial													
Exposure Scenario	**Crop or Target**	**App. Rate[a] (lb ai/ unit)**	**Area Treated[b] (units/ day)**	**Contract/Commercial** For risk management purposes, the currently labeled level of PPE and EC has been identified (shaded) for each individual exposure scenario.									
				SL/NoG No R	**SL/G NoR**	**DL/G No R**	**SL/NoG PF5 R**	**SL/G PF5 R**	**DL/G PF5 R**	**SL/No G PF10 R**	**SL.G PF10 R**	**DL/G PF10 R**	**EC**
Mixer/Loader/Applicators													
(10c) Wettable Powder: Mechanically -Pressurized Handgun PHED	Beef Cattle - Direct Spray	0.040 lb ai/animal	400 animals	4E-06	2E-06	2E-06	3E-06	1E-06	8E-07	3E-06	1E-06	7E-07	No Data
	Swine - Direct Spray	0.020 lb ai/animal		2E-06	1E-06	9E-07	1E-06	6E-07	4E-07	1E-06	5E-07	3E-07	No Data
	Poultry (Floor Management Litter, Fowl Tick), Poultry Droppings, Manure Piles, Garbage Piles, Under Feed Troughs	0.00080 lb ai/sq ft	20,000 sq ft	2E-05	1E-05	9E-06	1E-05	6E-06	4E-06	1E-05	5E-06	3E-06	No Data
	Poultry (Wire Cages) - Direct Spray	0.00040 lb ai/bird	20,000 birds	2E-06	1E-06	9E-07	1E-06	6E-07	4E-07	1E-06	5E-07	3E-07	No Data
	Dairy Barns, Poultry Houses, Swine Barns, or other Animal Buildings	0.00032 lb ai/sq ft	20,000 sq ft	8E-06	4E-06	4E-06	6E-06	2E-06	2E-06	6E-06	2E-06	1E-06	No Data
		0.00016 lb ai/sq ft		4E-06	2E-06	2E-06	3E-06	1E-06	8E-07	3E-06	1E-06	7E-07	No Data
		0.000080 lb ai/sq ft		2E-06	1E-06	9E-07	1E-06	6E-07	4E-07	1E-06	5E-07	3E-07	No Data

Exhibit Q

US Environmental Protection Agency Office of Pesticide Programs

EPA Reliance on Tetrachlorvinphos (TCVP) Data from Human Research on TCVP Exposure from Pet Collars

December 21, 2016

EPA Reliance on Tetrachlorvinphos (TCVP) Data from Human Research on TCVP Exposure from Pet Collars

Purpose

In compliance with EPA's rule for protection of human subjects, specifically 40 CFR 26.1706(d), EPA is hereby publishing its full explanation of the Agency's decision to rely on data from human research on tetrachlorvinphos (TCVP) exposure from pet collars. Relying on this data is crucial to EPA's decision that more stringent regulatory restrictions are necessary to protect public health than could be justified without the data.

EPA's Registration Review of TCVP

EPA is conducting its registration review of TCVP pursuant to section 3(g) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), 7 U.S.C. 136a(g), and the regulations concerning registration review at 40 CFR Part 155, subpart C. Section 3(g) of FIFRA provides, among other things, that the registrations of pesticides are to be reviewed every 15 years. Under FIFRA, a pesticide product may be registered or remain registered only if it meets the "[no] unreasonable adverse effects on the environment" standard for registration under FIFRA sections 2(bb) and 3(c), 7 U.S.C. §§ 136(bb) and 136a(c). That is, when used in accordance with widespread and commonly recognized practice, the pesticide product must perform its intended function without unreasonable adverse effects on man or the environment, and without posing a human dietary risk from residues that result from the use of a pesticide in or on food under the "reasonable certainty [of] no harm" standard of section 408(b)(2) of the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 U.S.C. § 346a(b)(2).

EPA's Proposal to Rely on Published TCVP Human Research

During the public meeting of the Human Studies Review Board (HSRB) held on January 12-13, 2016, EPA's Office of Pesticide Programs provided an overview and science and ethics review of the research discussed in the article "Assessing Intermittent Pesticide Exposure From Flea Control Collars Containing the Organophosphorus Insecticide Tetrachlorvinphos (TCVP)." This research article was authored by M. Keith Davis, J. Scott Boone, John E. Moran, John W. Tyler and Janice E. Chambers and published in 2008 in the *Journal of Exposure Science and Environmental Epidemiology* (2008) 18, pages 564-570. EPA presented the Davis et al. research to the HSRB for their review, along with a request for the HSRB to respond to questions posed by EPA.

The Davis et al. research measured TCVP exposures in children and adults that could occur from contact with pet dogs wearing TCVP-containing flea control collars. The research was based on two studies conducted by the Center of Environmental Health Sciences, College of Veterinary Medicine, Mississippi State University (MSU). Although the families involved in the studies already used flea collars, the researchers provided specific flea collars to the participating families and asked that their dogs wear them during the studies.

In study 1, conducted in 1998, TCVP residues were measured by rubbing/petting dogs' fur

with a gloved hand. The sampling was conducted by volunteer technicians from MSU veterinary school who stroked the animals in a standardized, prescribed manner, in a marked 10 x 4 inch area with clean, white, cotton gloves for a continuous 5-minute period. The dogs were rubbed in three specific locations: near the base of the tail, at the neck with the flea collar removed, and at the neck with the flea collar in place. Study 1 also measured dog plasma cholinesterase. There were 23 pet dogs included in this study, one from each of the 23 participating households.

Under study 2, conducted in 2002, volunteer technicians from MSU veterinary school collected TCVP residues by rubbing/petting dogs' fur with a gloved hand, and used the same methods as those employed by study 1. The collection of the glove residue data did not involve children in either study 1 or study 2. However, study 2 also quantified TCVP residues on tee shirts worn by children and included biomonitoring of the TCVP metabolite 2,4,5-trichloromandelic acid (TCMA) in urine of participating children and adults. Study 2 included 1 child and 1 adult from each of the 22 participating families and 22 pet dogs.

EPA is using only the glove residue data from the Davis et al. research in its risk assessment of TCVP because it is chemical-specific and results in the highest computed risks when compared to other available pet collar exposure data and all the approaches considered in the assessment; as a result, it supports the most protective risk outcomes. The research complied with the ethical standards in place at the time the studies were conducted and meets the substantive acceptance standards. As described in the Davis et al. research, the data were derived in a manner that makes the research scientifically valid and appropriate for use in EPA's risk assessment.

In the Federal Register of January 20, 2016 (81 FR 3128, FRL-9940-81), EPA sought public comment on EPA's draft human health and ecological risk assessment for the registration review of TCVP. The public can view the draft human health risk assessment and supporting documents, as well as comments received, in the docket established for the reregistration review of TCVP (see docket ID number EPA-HQ-OPP-2008-0316). EPA has determined that relying on the glove residue data from the Davis et al. research is crucial to EPA's decision that more stringent regulatory restrictions are necessary to protect public health than could be justified without the data. EPA currently does not have other pet collar glove residue data which are chemical-specific or that would lead to the same regulatory action to improve public health protection. For this reason, the glove residue data are crucial to EPA's decision.

Reason for Review by the HSRB

EPA chose, in this case, to obtain the views of the HSRB concerning EPA's proposal to rely on the TCVP glove residue data from studies 1 and 2 for the following reasons. First, the proposal submitted to EPA's Science to Achieve Results (STAR) grants program for funding of the research discussed correlating the residues from the rubbing procedure with the gloves, the residues from the tee shirts worn by children participating in the studies, and the urinary metabolites of the children and adults in the participating households and described these activities under the umbrella of one research project. Moreover, although EPA is relying only

on the TCVP glove residue data from both studies, study 2 further involved children wearing tee shirts and providing urine samples, and, at least for that portion of the study, is considered research involving intentional exposure to human subjects. Therefore, even though EPA does not wish to rely on the data involving children (namely the tee shirt and urinary data), EPA chose in this case to assume that the prohibition in 40 CFR 26.1703 and the process in 40 CFR 26.1706 apply, including submission of the research to the HSRB for review.

40 CFR 26.1703 prohibits EPA reliance on data from any research involving intentional exposure of any human subject who is a pregnant woman (and therefore her fetus), nursing woman, or child, except as provided in 40 CFR 26.1706. 40 CFR 26.1706 explains that EPA may rely on data that are unacceptable under the standards in 40 CFR 26.1703 through 26.1705 only if EPA has: (a) obtained the views of the HSRB; (b) provided an opportunity for public comment on the proposal to rely on the otherwise unacceptable data; (c) determined that relying on the data is crucial to a decision that would impose a more stringent regulatory restriction to protect public health than could be justified without the data; and (d) published a full explanation of the decision to rely on the data, including a thorough discussion of the ethical deficiencies of the underlying research and the full rationale for finding that the standard in item (c) was met.

EPA sought and obtained the views of the HSRB, discussed below, during the public HSRB meeting on January 12-13, 2016. The HSRB documented their views in meeting minutes, certified on February 24, 2016, and a final report, issued on March 30, 2016, before EPA published this explanation required by 40 CFR 26.1706(d). The final report is available at: https://www.epa.gov/osa/hsrb-january-12-13-2016-meeting-final-report

Public Opportunity to Comment on EPA's Proposal to Rely on Data

Pursuant to 40 CFR 26.1706(b), in the Federal Register (FR) of April 11, 2016 (81 FR 21335, FRL-9944-37), EPA provided an opportunity for public comment on EPA's proposal to rely on the TCVP glove residue data from the Davis et al. research. The FR Notice is accessible at https://www.gpo.gov/fdsys/pkg/FR-2016-04-11/pdf/2016-08281.pdf and provided the following information: EPA's proposal to rely on the Davis et al. research; the reason for review by HSRB; the background on ethical conduct of research; summary of discussion on ethics-related questions; the standards applicable to ethical conduct and reliance on data; and the availability of HSRB meeting materials. EPA proposed to rely on the data in order to impose a more stringent regulatory restriction that would improve public health protection than could be justified without relying on the data and solicited public comment.

EPA received 4 public comments in response to the FR Notice. No substantive comments objected to EPA's reliance upon the Davis et al. research.

The public can view all four comments in the regulations.gov docket ID number EPA-HQ-OPP-2008-0316 at https://www.regulations.gov/docket?D=EPA-HQ-OPP-2008-0316.

Background on Ethical Conduct of Research

The Davis et al. research was funded by EPA's STAR grants. EPA's Office of Research and Development (ORD) reviewed the grant proposal, which involved human research and funding from EPA. EPA's ethics review of the Davis et al. research presented at the January 2016 HSRB meeting relies in part on EPA's ORD file because it contains draft consent forms used during study 2 and recruitment information. At the January 2016 HSRB meeting, EPA discussed the role of the veterinary students, the societal value of the Davis et al. research, and ethical considerations regarding recruitment of study participants, the independent ethics review, informed consent, respect for subjects and compensation for participation in the study.

EPA reviewed with the HSRB the role of the veterinary students in rubbing the dogs. The technicians who rubbed the dogs in study 1 and study 2 were students enrolled at MSU's College of Veterinary Medicine. Both the researchers and the Institutional Review Board (IRB) viewed the veterinary students as technicians in the study, not as human subjects. The abstract for the research submitted to EPA for funding is included in the ORD file and states, on page 14, that "the samplers will be trained so that consistency in the sample collection is maintained among dogs and among samplers." As discussed in the research article, the technicians wore gloves and stroked the animals in a standardized, prescribed manner: "in a marked 10 x 4 inch area with clean, white, cotton gloves for a continuous 5-min period." The dogs were rubbed in specific locations (near the base of the tail, at the neck with collar removed, and at the neck with the collar in place). Under 40 CFR 26.1102(e), the term "human subject" is defined, in part, as "a living individual about whom an investigator … conducting research obtains … [d]ata through intervention or interaction…." The Primary Investigator for the research confirmed that she did not obtain data about the technicians, nor did she intend to do so. The pattern of rubbing does not resemble the typical human-pet interaction or provide information about how a person would normally interact with a pet. EPA noted during the HSRB meeting that the researchers were not collecting data about the technicians in this study and concluded that there is no indication from the research article, the ORD file or EPA's interview with the Primary Investigator (PI) that the study collected data about the veterinary students who worked as technicians in the study. Instead, the researchers collected data only about the residues on the glove as an indication of how much residue was available for transfer from the pet.

With regard to the societal value of the Davis et al. research, the objective was to assess the amount of exposure to TCVP that could occur in children and adults from the use of a TCVP-containing collar on a pet dog. Regarding recruitment, the research article states that "the studies were conducted in Oktibbeha County, Mississippi (USA), with volunteer households having pet dogs" and that "participating families were volunteers who routinely used flea control products on their pet dogs." "One child and one adult were selected from each participating family" for study 2, which included 44 subjects. EPA's file on the STAR grant, page 13, states that: "Dogs selected for this study will be owned by professional (DVM) or graduate students enrolled in the College of Veterinary Medicine, or staff/faculty members of Mississippi State University with a child aged 4-10 years in the household who routinely plays with this dog." It goes on to state that "[s]tudents or staff should be the most

reliable group of owners (in contrast to the general public) in that they are accessible daily, their dogs can readily be treated and sampled when the students are in class or the staff members are at work, and as members of the academic community, the compliance and appreciation of the value of research should be high." EPA's file further states that "[d]ogs participating in this study must be enrolled in the Small Animal Community Practice Health Maintenance Program, so that their health status and vaccination history are known."

Regarding the independent ethics review, the IRB for Research on Human Subjects at MSU reviewed and approved the sampling protocols and consent forms, and the EPA's ORD, the National Center for Environmental Research and Quality Assurance (NCERQA) reviewed the STAR grant proposal focusing on this research. ORD supported the research dependent on the incorporation of NCERQA comments on the consent forms. The protocol was distributed to each participating household, informed consent was obtained from the adults, and children were informed verbally of the procedures and oral or written assent was obtained from them. The IRB for Research on Human Subjects at MSU approved all sampling protocols and informed consent forms. The ORD file contains a draft consent form for adults and a Minor's Assent Form. The consent form states that the study involves research and identifies its purpose, expected duration, number of urine and tee shirt samples to be provided, states that research results will be coded, participants are free to withdraw, provides a contact for information, and specifies compensation of $150 for each participating household. The consent form, entitled "Authorization for Participation in Research Project," also states that "no risks are anticipated to the participants." The implication is that since families already used flea collars on their dogs, there was no added risk from participating in the study. In the abstract that the researchers submitted to ORD, however, page 4 states that "the residues of insecticides available for intermittent transfer to children from the fur of dogs treated by either a spot treatment or a collar for flea control will be appreciable and of a magnitude necessitating inclusion in cumulative risk assessments of pesticides to children; secondly, that the fur rubbing procedure developed to quantify dislodgeable residues provides a useful estimate of insecticide residues which could be transferred from the fur of dogs to children."

Although the families involved already used flea collars registered by EPA, in the interest of transparency, it would have been preferable for the researchers to have shared their aforementioned hypothesis with the parents of the participating children and included it in the consent form. It is unknown whether the information was stated in the protocol provided to the families. The Minor's Assent Form states that the researchers "will specifically obtain assent from the children recruited to our project...We will explain that the child's parent or guardian has given us permission to request his/her help participation (sic) in the research project. We will then explain the urine collection protocol and the tee shirt protocol to the children in language appropriate to the age of the child and obtain his/her assent to participate. We will not explain the connection to the pesticide residues on the dog so as not to alter the behavior of the child with the dog. We will obtain the children's assent orally because of the age range of the children involved."

The researchers demonstrated respect for subjects participating in the study in several ways. The researchers: did not reveal subjects' identities; obtained informed consent from

participating subjects; provided light weight short-sleeve tee shirts to children for use during the study; gave written assurance that urine samples would only be used to quantify insecticide urinary metabolites; and provided compensation for participation in the study. Compensation included $100 equivalent of veterinary care provided by the Animal Health Center of MSU College of Veterinary Medicine and $150 to participating households in Study 2.

Summary of Discussion on Ethics-Related Questions

As documented on page 6 of the final report of the January 2016 HSRB meeting, in response to EPA's science charge question, the HSRB stated that, "The research is scientifically sound and, if used appropriately, the pet fur transferable residue data from the rubbing protocol used in the study can provide useful information for evaluating potential exposures of adults and children from contact with dogs treated with tetrachlorvinphos containing pet collars." The HSRB final report also includes the HSRB's detailed recommendations and rationale. The final report, on page 9 in the science review section, explains that:

> There are a number of limitations related to the studies published in Davis et.al. (2008) that are mostly related to a lack of information and details which are not available to the Agency. The limitations identified by the HSRB are listed at the end of this section. However, despite these limitations, the data as presented are sufficiently sound to support an estimate of the Far^1 if the maximum transferable residue is used. The data is less satisfying for averaging over the duration of each study but can still support screening assessments.

The only science limitations identified by the HSRB are listed on pages 10-11 of the final report as follows:

> Additional notes on scientific issues identified in review of the Davis et.al. (2008) paper:
> 1. The application rate of active ingredient is assumed to be the same for all dogs regardless of size/weight (i.e., 4.8 grams per dog). The Agency requested information from the principal investigator of the study, but the information is not available.
> 2. Assuming that the application rate was the same on all dogs, it is unclear how the long tails on the collars were handled on the small dogs and whether the long tail on the collar could be contacted by the glove during petting. If the collar was tucked in behind and wrapped multiple times around the neck then it would potentially bias the transferable residue upwards.
> 3. The original data from the study are not available. A lack of information about dog size and individual glove data prevents any statistical assessment of the results beyond what is already reported (which is minimal with respect to the residue transfer data).

[1] i.e., the fraction of the pet collar application rate available as transferable residue

4. It is assumed that the five minute petting events remove all of the transferable residue without the gloves becoming saturated and without significant leaching through to the skin of the research staff undertaking the data collection.
5. Information is lacking to assess the relationship between transferable residue and dog size, type, hair which would be important to estimate worst case *Far* values.
6. It is unknown whether there is any loss of active ingredient through the cotton gloves to the technicians' hands. This loss would reduce the value of transferable residue and in turn reduce the resulting *Far*.

For more information, the minutes and final report of the January 12-13, 2016 public HSRB meeting are available on the HSRB website at *http://www.epa.gov/osa/january-12-13-2016-meeting-human-studies-review-board*. The science review is pertinent to the ethics discussion because if a study is not scientifically sound, then it is not ethical to rely on it; that is not the case here because both EPA and the HSRB determined that the research is scientifically sound.

Regarding the topic of ethical deficiencies of the research, as previously discussed, the researchers' hypothesis was described in the research abstract submitted to EPA's Office of Research and Development and states, in part, that "the residues of insecticides available for intermittent transfer to children from the fur of dogs treated by either a spot treatment or a collar for flea control will be appreciable and of a magnitude necessitating inclusion in cumulative risk assessments of pesticides to children." Although the families involved already used flea collars registered by EPA, in the interest of transparency, it would have been preferable for the researchers to have shared their hypothesis with the parents of the participating children and included it in the consent form. It is unknown whether the information was stated in the protocol provided to the families. EPA believes that the researchers not sharing their hypothesis with the parents of participating children was an ethical deficiency of the study. EPA also posed two ethics charge questions to the HSRB related to this research.

First, EPA asked the Board, "Does the HSRB have any comments on EPA's determination that the samplers were not human subjects?" The HSRB's response is discussed on pages 11-12 of the HSRB's final report and reads as follows:

> With regard to the first charge question, questions were raised by several committee members about the PI's and IRB's determinations that the samplers were not human subjects in the study; rather, they were viewed as study staff. Some members of the board asserted that the student/technicians, by virtue of being potentially exposed to the pesticide as part of the conduct of the study, should have been considered human subjects. Furthermore, if they had been treated as subjects, they might have been considered 'vulnerable' due to their status as students. It was noted that the flea control collars were commercially available at the time, and that the potential exposure to the pesticide residues through petting the dogs

> for five minute periods wearing cotton gloves was likely much less than average exposure of a pet owner. There is no information available about whether there was any 'bleed through' of pesticide from cotton gloves to the skin of the samplers and therefore the actual exposure is unknown. Considering all of these factors, the committee felt that the risks of exposure were not greater than those experienced in everyday life. Thus, even if the determination regarding the status of the samples as study staff rather than subjects was mistaken, the committee did not believe this resulted in any material harms and so this question should not prevent the EPA from using the pet fur transferable residue data derived from the study for making a decision to impose a more stringent regulatory restriction than could be justified without the data.

EPA also asked the HSRB if they had any comments on the ethical conduct of the research. As documented on pages 12-13 of the HSRB's final report:

> With regard to the second charge question, Board members observed that the records from correspondence with EPA staff regarding the study suggest the consent form was amended to include disclosure to parents about the risks of pesticide exposure, although the final approved consent form was not provided. A question was raised about the decision made to provide incomplete assent to the minor subjects following parental permission. Study documents suggest this was an intentional choice ('We will not explain the connection to the pesticide residues on the dog…'), which was made, according to study documents, in order to avoid confounding the results by causing alterations in the children's behavior around their dogs. Board members noted that the amount and type of information provided to children in an assent process will vary depending on the age of the child; the children participating in the study were between the ages of 3 and 11 years old and therefore would have had varying levels of capacity to process the information about the study. It was noted that the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), which existed at the time of these studies, states that it's unlawful to use any pesticide in tests on humans unless they are fully informed of the nature and purposes of the test. Although some board members viewed the assent as incomplete in this case, because parents are presumed to have given fully-informed permission, and given that the flea control collars were commercially available at the time and already in use in the households recruited to the study, the committee felt that the risks of exposure were not greater than those experienced in everyday life. Thus, the committee did not believe this resulted in any material harms and so this question should not prevent the EPA from using the pet fur transferable residue data derived from the study for making a decision to impose a more stringent regulatory restriction than could be justified without the data.

Summary of Scientific Rationale for EPA's Decision to Rely on Data

As discussed above, the HSRB concluded that, "The research is scientifically sound and, if used appropriately, the pet fur transferable residue data from the rubbing protocol used in the study can provide useful information for evaluating potential exposures of adults and children from contact with dogs treated with tetrachlorvinphos containing pet collars." As the HSRB has determined that the Davis et al. research is scientifically valid and meets appropriate human ethics requirements, EPA is relying on these data for regulatory decision making since these data demonstrate greater potential risks than those estimated using the amitraz pet collar residue transfer study (which had been relied upon in the previous risk assessments). Accordingly, residential post-application risks to adults and children following contact with pets treated with TCVP pet collars have been assessed with use of the data from the Davis et al. research only.

The use of the Davis et al. research as the primary data source is consistent with, and supported by, the recommendations from the comments following EPA's 2015 Occupational and residential exposure (ORE) assessment, including those submitted by the Natural Resources Defense Council (NRDC) and the Hartz Mountain Corporation. Per NRDC, "the Davis Study has met the appropriate scientific and ethical criteria and should be relied upon for the evaluation of exposures from TCVP containing flea collars," and the Hartz Mountain Corporation states that, "the glove residue data measured in the Davis et al. (2008) study are valuable because they represent actual measurements of TCVP transfer from dogs wearing commercial collars to the hands of individuals petting them." Further, the NRDC states that "EPA's utilization of transferable residue data from the amitraz study is not supported by the evidence and should not be relied upon to evaluate risk." In summary, for the reasons described above, EPA has decided to rely on the glove residue data from Davis et al., given that it is crucial to EPA's decision that more stringent regulatory restrictions are necessary to protect public health than could be justified without the data. The implications of the Davis et al. research will be discussed in the Agency's registration review Proposed Interim Decision for TCVP, which EPA expects to publish for a 60-day public comment period in 2017.

Standards Applicable to Ethical Conduct and Reliance on Data

With regard to the standards applicable to the conduct of the research, study 1 was conducted in 1998 and study 2 was conducted in 2002, both before EPA's Rule for Protection of Human Subjects (40 CFR Part 26, subparts B through Q) became effective in 2006. Thus, 40 CFR Part 26, subparts B through Q, did not apply when this research was conducted. However, EPA's codification of the Common Rule at 40 CFR Part 26 subpart A was in place and applies to the underlying research that received EPA's STAR grant funding. Key elements of the Common Rule include IRB oversight and prior approval, an acceptable informed consent process, risk minimization, a favorable risk-benefit balance, equitable subject selection, and fully informed and voluntary participation by subjects. In addition, FIFRA section 12(a)(2)(P), which states that it is unlawful to use any pesticide in tests on humans unless they are fully informed of the nature and purposes of the tests, as well as of any reasonably foreseeable physical and mental health consequences, and that participants freely volunteer, existed at the time of these studies. The Davis et al. research complied with the standards in

place at the time the research was conducted.

The substantive acceptance standards which apply to the research include: 40 CFR 26.1703, which, except as provided in 40 CFR 26.1706, prohibits relying on data involving intentional exposure of pregnant or nursing women or of children; 40 CFR 26.1704, which, except as provided in 40 CFR 26.1706, prohibits reliance on data if research was fundamentally unethical or deficient relative to prevailing standards at the time; and FIFRA section 12(a)(2)(P), which makes it unlawful to use a pesticide in human tests without fully informed, fully voluntary consent. 40 CFR 26.1706 states that EPA may rely on data that are unacceptable under the standards in 40 CFR 26.1703 through 26.1705 only if EPA has: (a) obtained the views of the HSRB, (b) provided the opportunity for public comment on the proposal to rely on the otherwise unacceptable data, (c) determined that relying on the data is crucial to a decision that would impose a more stringent regulatory restriction to protect public health than could be justified without the data, and (d) published a full explanation of the decision to rely on the data, including a thorough discussion of the ethical deficiencies of the underlying research and the full rationale for finding that the standard in item (c) was met.

Regarding 40 CFR 26.1703, study 2 involved tee shirt and urine samples that came from children. As explained previously, even though EPA only intends to rely on the glove residue data from study 1 and study 2, which did not involve children, EPA chose in this case, out of an abundance of caution, to proceed under 40 CFR Part 26, subpart Q.

Regarding 40 CFR 26.1704, clear and convincing evidence that the pre-rule research was fundamentally unethical or deficient relative to prevailing ethics standards does not exist, and the research complied with FIFRA section 12(a)(2)(P). In satisfaction of 40 CFR 26.1706(a), EPA sought and obtained the views of the HSRB during the public HSRB meeting on January 12-13, 2016. The HSRB had already documented their views in meeting minutes and a final report before EPA published this explanation as required by 40 CFR 26.1706(d). Pursuant to 40 CFR 26.1706(b), EPA provided an opportunity for public comment on EPA's proposed decision to rely on the glove residue data.

Regarding 40 CFR 26.1706(c), EPA has determined that relying on the glove residue data from the Davis et al. research is crucial to EPA's decision that more stringent regulatory restrictions are necessary to protect public health than could be justified without the data, as explained in EPA's draft human health and ecological risk assessment for the registration review of TCVP.

Regarding 40 CFR 26.1706(d), the posting of this explanation on EPA's public website fulfills the requirements of 40 CFR 26.1706(d). In addition, EPA intends to post this explanation to docket number EPA-HQ-OPP-2008-0316 in regulations.gov and notice its availability in EPA's Federal Register (FR) Notice associated with the final TCVP human health risk assessment.

Availability of HSRB Meeting Materials

In accordance with the requirements of the Federal Advisory Committee Act (FACA), 5 U.S.C. Appendix 2, the minutes of the HSRB public meeting held on January 12-13, 2016, including a description of the matters discussed and conclusions reached by the Board, were certified by the HSRB meeting Chair and made public within 90 days of the meeting. The HSRB meeting Chair certified those meeting minutes on February 24, 2016. The HSRB prepared a final report, dated March 30, 2016, which responded to questions posed by the EPA and included the Board's review and analysis of materials presented. The approved minutes, final report and other materials from the January 12-13, 2016 HSRB meeting are available on the HSRB website at *http://www.epa.gov/osa/human-studies-review-board*.

Other Related Information on TCVP

The public can view EPA's draft human health and ecological risk assessment and supporting documents for the registration review of TCVP in the docket at *http://www.regulations.gov* (see docket ID number EPA-HQ-OPP-2008-0316). Information on the Agency's registration review program and its implementing regulation is available at *https://www.epa.gov/pesticide-reevaluation/registration-review-process*. EPA anticipates finalizing the TCVP registration review human health risk assessment in 2016 and discussing the implications of the Davis et al. research in the Agency's TCVP Proposed Interim Decision (PID), which EPA expects to publish for public comment in 2017.

Exhibit R

EPA United States Environmental Protection Agency

EPA Finalizes Human Health Risk Assessment for Pesticide Used on Pets

For Release: January 4, 2017

EPA has finalized the human health risk assessment of tetrachlorvinphos (TCVP). TCVP is an organophosphate insecticide used to control fleas, ticks, and other pests on and around pets and livestock. It is used in residential products like pet collars.

Through the publication of the revised human health risk assessment and related documents, we are addressing a 2009 Natural Resource Defense Council (NRDC) petition.

This risk assessment identified potential risks to people, including children, in residential settings and to certain workers applying TCVP, which exceed the Agency's level of concern.

The Agency has contacted the pesticide manufacturers to initiate discussions with them to reduce exposure and resolve potential risks identified in the human health risk assessment. The Agency will issue a Proposed Decision in 2017 for public comment. Until that time, it is important to follow label instructions on proper use of pesticide products.

We advise consumers to take certain precautions when handling TCVP products in residential areas. These precautions are listed on TCVP product labels, including:

- not allowing children to play with TCVP pet collar products,
- keeping TCVP spray and powder products out of reach of children, and
- washing hands thoroughly with soap and water after handling.

To view TCVP's human health risk assessment and other registration review documents, visit regulations.gov, docket number EPA-HQ-OPP-2008-0316.

More information on:

- tetrachlorvinphos
- protecting your pets form fleas and ticks
- reducing your child's chances of pesticide poisoning

Exhibit S

Message

From: Zilioli, Erica (ENRD) [Erica.Zilioli@usdoj.gov]
Sent: 3/9/2017 11:19:15 PM
To: Ian Fein [ianfein@gmail.com]
CC: Wakefield, Benjamin J. [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b2756b86404b49448581918fd2fbc13c-BWAKEFIE]; mwu@nrdc.org
Subject: RE: Tetrachlorvinphos (TCVP) Revised Human Health Risk Assessment

Flag: Follow up

Hi Ian,

EPA currently intends to send something to NRDC by March 21st.

Thanks,
Erica

Erica M. Zilioli
U.S. Department of Justice
Environmental Defense Section
P.O. Box 7611
Washington, DC 20044
202.514.6390

From: Ian Fein [mailto:ianfein@gmail.com]
Sent: Thursday, March 02, 2017 11:25 PM
To: Zilioli, Erica (ENRD) <EZilioli@ENRD.USDOJ.GOV>
Cc: Wakefield, Benjamin J. <wakefield.benjamin@epa.gov>; mwu@nrdc.org
Subject: Re: Tetrachlorvinphos (TCVP) Revised Human Health Risk Assessment

Thank you so much, Erica. Next week would be great.

I should have new contact info soon, and will pass it along when I do. In the meantime, you can reach me at this email address and my cell phone, 415-367-5062.

Thanks again,
Ian

On Mar 2, 2017, at 12:39 PM, Zilioli, Erica (ENRD) <Erica.Zilioli@usdoj.gov> wrote:

> Hi Ian,
>
> Congratulations on making a move! Please send us your new contact info once you have it.
>
> I am pretty swamped this week getting some filings done in another case but I will confer with EPA about the status of TCVP and hopefully get back to you with an update early next week.
>
> Thanks,
> Erica

Erica M. Zilioli
U.S. Department of Justice
Environmental Defense Section
P.O. Box 7611
Washington, DC 20044
(202) 514-6390
erica.zilioli@usdoj.gov

From: Fein, Ian [mailto:ifein@orrick.com]
Sent: Tuesday, February 28, 2017 5:05 PM
To: Wakefield, Benjamin J. <wakefield.benjamin@epa.gov>
Cc: Zilioli, Erica (ENRD) <EZilioli@ENRD.USDOJ.GOV>; mwu@nrdc.org; ianfein@gmail.com
Subject: RE: Tetrachlorvinphos (TCVP) Revised Human Health Risk Assessment

Hi Ben and Erica,

I hope you've both been well. I wanted to thank you again for giving us a head's up about the TCVP Risk Assessment back in December, and also to check in and see whether you had any further updates on the process.

Is it still EPA's intention to issue a final revised response to NRDC's 2009 petition within 90 days of the December issuance of the Risk Assessment?

Also, I am leaving my current firm but will continue to be working with NRDC on this case. So for future correspondence on this matter, please email me at ianfein@gmail.com.

Many thanks again,
Ian

From: Wakefield, Benjamin J. [mailto:wakefield.benjamin@epa.gov]
Sent: Wednesday, December 28, 2016 3:39 PM
To: Fein, Ian <ifein@orrick.com>
Cc: Erica Zilioli <Erica.Zilioli@usdoj.gov>; mwu@nrdc.org
Subject: RE: Tetrachlorvinphos (TCVP) Revised Human Health Risk Assessment

Ian,

It is EPA's current intention and belief that the Agency will issue a final revised response to NRDC's 2009 petition to cancel all pet uses of TCVP within 90 days of issuing the Revised Human Health Risk Assessment for Registration Review.

The Revised Risk Assessment is not yet public, and it will speak for itself regarding the Davis Study when it is posted to the regulations.gov docket.

I do not currently have a precise estimate of when the Proposed Interim Decision is likely to be published.

Have a Happy New Year.

Regards,

- Ben

Benjamin J. Wakefield
U.S. Environmental Protection Agency
Office of General Counsel, Pesticides & Toxic Substances Law Office
1200 Pennsylvania Ave., N.W., Mail Code 2333A
Washington, D.C. 20460
Tel: 202-564-3186
Fax: 202-564-5531
wakefield.benjamin@epa.gov

From: Fein, Ian [mailto:ifein@orrick.com]
Sent: Wednesday, December 28, 2016 6:22 PM
To: Wakefield, Benjamin J. <wakefield.benjamin@epa.gov>
Cc: Erica Zilioli <Erica.Zilioli@usdoj.gov>; mwu@nrdc.org
Subject: RE: Tetrachlorvinphos (TCVP) Revised Human Health Risk Assessment

Thanks so much for the heads up, Ben. We really appreciate it. I hope you and Erica have both had a wonderful holidays so far.

Now that the risk assessment has been finalized, does EPA still plan to revise its response to NRDC's cancellation petition within 90 days?

Also, we saw the document posted on the docket last week about EPA's decision to rely on the Davis Study. Will the risk assessment discuss the "more stringent regulatory decisions" referenced in that document, or will that be in the Proposed Interim Decision (PID) instead? And do you know when in 2017 the PID will likely be published for public comment?

Thanks again for reaching out. I hope you and Erica each have a wonderful time away from the office.

Best,
Ian

From: Wakefield, Benjamin J. [mailto:wakefield.benjamin@epa.gov]
Sent: Wednesday, December 28, 2016 12:39 PM
To: Fein, Ian <ifein@orrick.com>; mwu@nrdc.org
Cc: Erica Zilioli <Erica.Zilioli@usdoj.gov>
Subject: Tetrachlorvinphos (TCVP) Revised Human Health Risk Assessment

Ian and Mae,

The Tetrachlorvinphos (TCVP) Revised Human Health Risk Assessment for Registration Review has been finalized and is in the process of being posted to the TCVP registration review docket at regulations.gov (https://www.regulations.gov/docket?D=EPA-HQ-OPP-2008-0316). Although the revised risk assessment does not yet appear to be posted to the docket, I expect that it will be in the next few days.

I will be out of the office starting tomorrow, returning Tuesday, January 3rd. Erica is out until Monday, January 9th. Since both of us will likely be out of the office when the document posts to the docket, I wanted to let you know that the document has been finalized in case you wish to monitor the docket for its posting.

Regards,

- Ben Wakefield

Benjamin J. Wakefield
U.S. Environmental Protection Agency
Office of General Counsel, Pesticides & Toxic Substances Law Office
1200 Pennsylvania Ave., N.W., Mail Code 2333A
Washington, D.C. 20460
Tel: 202-564-3186
Fax: 202-564-5531
wakefield.benjamin@epa.gov

From: Zilioli, Erica (ENRD) [mailto:Erica.Zilioli@usdoj.gov]
Sent: Tuesday, June 14, 2016 2:45 PM
To: Wakefield, Benjamin J. <wakefield.benjamin@epa.gov>
Subject: FW: TCVP case

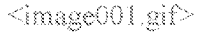
FYI.

From: Weaver, Susannah Landes [mailto:sweaver@orrick.com]
Sent: Tuesday, June 14, 2016 2:39 PM
To: Zilioli, Erica (ENRD) <EZilioli@ENRD.USDOJ.GOV>
Cc: Fein, Ian <ifein@orrick.com>
Subject: TCVP case

Hi Erica,

I hope you're doing well. I wanted to let you know that I will be leaving Orrick tomorrow to join Donahue & Goldberg. For any further communications on the TCVP matter, Ian Fein (cc'd here) will be the point person.

Best,
Susannah



SUSANNAH LANDES WEAVER
Attorney at Law

ORRICK, HERRINGTON & SUTCLIFFE LLP
Orrick Building at Columbia Center
1152 15th Street NW
Washington, DC 20005-1706

Exhibit T

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

ELECTRONIC MAIL

March 21, 2017

Mae Wu, Esq.
Natural Resources Defense Council
1152 15th Street, NW, Suite 300
Washington, D.C. 20005

Re: Natural Resources Defense Council's April 23, 2009 Petition Requesting Cancellation of All Pet Uses of Tetrachlorvinphos

Dear Ms. Wu:

On December 21, 2016, the U.S. Environmental Protection Agency (EPA) finalized a "Tetrachlorvinphos (TCVP) Revised Human Health Risk Assessment for Registration Review," available at https://www.regulations.gov/document?D=EPA-HQ-OPP-2008-0316-0055. EPA intends to address any risk-mitigation issues for the pet-care uses of TCVP when it addresses risk-mitigation issues for all TCVP products in the course of registration review for the chemical, pursuant to section 3(g) of the Federal Insecticide, Fungicide, and Rodenticide Act, 7 U.S.C. § 136a(g).

Please contact Khue Nguyen at (703) 347-0248 or nguyen.khue@epa.gov, if you have any questions or concerns.

Sincerely,

Yu-Ting Guilaran, Director
Pesticide Re-evaluation Divison

Exhibit U

Registration Review Schedules

Through the Pesticide Registration Review program, EPA reviews all registered pesticides at least every 15 years, as mandated by the Federal Insecticide, Fungicide, and Rodenticide Act.

EPA always strives to base its decisions on the best available sound science. However, science is constantly evolving, and new scientific information can come to light at any time and change our understanding of potential risks from pesticides. The review of new data could potentially prolong the risk assessment and decision-making process and change this schedule.

The schedule below shows the status of pesticides undergoing registration review. This schedule is subject to change based on shifting priorities and is intended to be a rough timeline. We will update the schedule regularly to reflect any timeline changes and to include anticipated deliverables for later dates.

Explanation of List

The registration review process includes:

- Docket Openings
- Draft Risk Assessments
- Proposed Interim Decisions / Proposed Decisions
- Interim Decisions / Decisions

EPA commits to an open and transparent process by accepting public comments at most stages of the process. These are collected in each chemical's docket at www.regulations.gov and all comments submitted will be accounted for in the Agency's regulatory decisions for each chemical.

The schedule is also categorized by the fiscal year's (FY) quarters. Please note the following timeframes:

- Quarter 1 (Q1): October - December
- Quarter 2 (Q2): January - March
- Quarter 3 (Q3): April - June
- Quarter 4 (Q4): July - September

Registration Review Schedules

2017 Registration Review Schedule for Conventional Cases (as of 02/09/2017)

2017 Registration Review Schedule for Conventional Cases (as of 02/09/2017)

Draft Risk Assessments	Proposed Interim Decisions	Interim Decisions
Quarter 1		
• 2,4-D (Eco Only) • Bromacil • Chlorethoxyfos • Clothianidin (Pollinator only) • Cyphenothrin • Cyprodinil • Dinotefuran (Pollinator only) • Imidacloprid (Aquatic only) • Phosmet • Propamocarb • Tetrachlorvinphos (Human health only) • Thiamethoxam (Pollinator only)		
Quarter 2		

2017 Registration Review Schedule for Conventional Cases (as of 02/09/2017)

- Acephate
- Benfluralin
- Bromuconazole
- Carbaryl (Human health only)
- Clodinafop-propargyl
- Chlorpyrifos (Biological evaluation only)
- Cyfluthrin (Human health only)
- Cypermethrin (Human health only)
- Diazinon (Biological evaluation only)
- Malathion (Biological evaluation only)
- Deltamethrin (Human health only)
- Dichlobenil
- Diflufenzopyr
- EPTC
- Esfenvalerate (Human health only)
- Imidacloprid (Human health only)
- Lufenuron
- Mepiquat chloride and mepiquat pentaborate
- Naled (Mosquito adulticide only)
- Nitrapyrin
- Pendimethalin
- Permethrin (Human health only)
- Phosmet
- Phostebupirim (Tebupirimiphos)
- Aldicarb
- Azoxystrobin (with Antimicrobial Division)
- Bifenazate
- Carfentrazone-ethyl
- Chlorpyrifos-methyl
- Coumaphos
- Ethalfluralin
- Pirimiphos-methyl
- Profenofos (case closure)
- Antimycin A
- Fosamine ammonium
- Flufenacet
- Flurprimidol
- Glufosinate
- Tebufenozide

2017 Registration Review Schedule for Conventional Cases (as of 02/09/2017)

Quarter 3

2017 Registration Review Schedule for Conventional Cases (as of 02/09/2017)

- 2,4-D (Human health only)
- Asulam
- Buprofezin
- Carbaryl (Biological evaluation only)
- Chlorpropham
- DCPA
- DDVP
- Etofenprox
- Glyphosate
- Gamma-Cyhalothrin (Human health only)
- Indoxacarb
- Lambda-Cyhalothrin (Human health only)
- Methiocarb
- Methomyl (incl. Biological evaluation)
- Metribuzin
- Naled (Human health only)
- Oryzalin
- Oxamyl
- Oxytetracycline
- Permethrin
- Piperonyl butoxide
- Prometryn
- Pyrethrins and derivatives (Human health only)
- Streptomycin
- Thiodicarb
- Trichlorfon
- Trifloxystrobin

- Copper Compounds: Group 2
- Copper Sulfate
- Copper Salts
- Spinosad
- Spinetoram

- Sulfonylurea (SU) herbicides
  - Bensulfuron-methyl
  - Chlorimuron-ethyl
  - Chlorsulfuron
  - Flazasulfuron
  - Foramsulfuron
  - Halosulfuron-methyl
  - Imazosulfuron
  - Iodosulfuron-methyl-sodium
  - Mesosulfuron-methyl
  - Metsulfuron-methyl
  - Nicosulfuron
  - Orthosulfamuron
  - Primisulfuron-methyl
  - Prosulfuron
  - Rimsulfuron
  - Sulfometuron-methyl
  - Sulfosulfuron
  - Thifensulfuron-methyl
  - Triasulfuron
  - Tribenuron-methyl
  - Trifloxysulfuron-sodium
  - Triflusulfuron-methyl

2017 Registration Review Schedule for Conventional Cases (as of 02/09/2017)

Quarter 4

- Abamectin
- Atrazine (Human health only)
- Bifenthrin (Human health only)
- Butralin
- Cloransulam
- Clothianidin
- Dinotefuran
- Emamectin Benzoate
- Fludioxonil
- Fluopicolide
- Fluridone
- Imidacloprid (ecological risk only)
- Norflurazon
- Propazine (Human health only)
- Pymetrozine
- Pyriproxyfen
- Quinoxyfen
- Simazine (Human health only)
- Terbacil
- Thiamethoxam

- Bromacil
- Chlorpyrifos
- Cyclanilide
- Cymoxanil
- Dimethomorph
- Flumiclorac-pentyl
- Kresoxim-methyl
- Linuron
- Metalaxyl
- MGK-264
- Propamocarb
- Tetrachlorvinphos

- Aldicarb
- Azoxystrobin (with Antimicrobial Division)
- Bifenazate
- Boric Acid (with Antimicrobial Division)
- Carfentrazone-ethyl
- Chlorpyrifos-methyl
- Clethodim
- Coumaphos
- Diquat Dibromide
- Ethalfluralin
- Ethephon
- Hexazinone
- Hymexazol
- Methoxyfenozide
- Pirimiphos-methyl
- Pronamide (Propyzamide)

LAST UPDATED ON FEBRUARY 14, 2017

Exhibit V

TCVP: notes and action items for 7/11/17 teleconference with Hartz

EPA indicated that it intended to publish the proposed interim registration review decision for TCVP in September 2017. The focus of the proposed decision is the pet uses. EPA is awaiting a final decision on the use of the 10X FQPA database uncertainty factor for all the organophosphates, and so the agency intends to address dietary, occupational, and eco risks at a later date.

Hartz thought implementing risk mitigation for pet uses was premature and thought there was room for refinement in EPA's current risk assessment. Hartz put forward several proposals for refinement via PowerPoint slides, including the use of adult biomonitoring data for children, use of information on timed contact with pets and frequency of contact with pets, and refining the mass balance estimates which is currently too conservative. EPA pointed Hartz to its most recent "response to comments" document for the occupational and residential assessment, where most of these comments were already addressed. EPA did not have a chance to examine the NERL data cited in Hartz' slides relating to contact with treated pets (i.e., number and duration of pet contacts), but indicated that Hartz should submit these studies as soon as possible, including any raw data.

EPA indicated that it was interested in data which might help refine the number and duration of pet contact inputs. EPA discussed recent registrant data for pet collars that sought to determine what fraction of the collar was liquid and what fraction was solid. Having access to similar data for TCVP could potentially impact the risk picture. Hartz was open to working with EPA on developing additional data, but was concerned about the September deadline.

EPA's timeline is spurred by its obligation to respond to NRDC's petition for the pet uses. EPA indicated that Hartz should submit a solid proposal describing what data will be developed and a timeline for the submission of this data in the next few weeks. EPA does not have flexibility to extend the September deadline without more concrete information. Hartz said it needed to discuss internally. Hartz agreed to submit a letter of intent with a proposed timeline for the key elements discussed by Tuesday 7/18.

Action items from teleconference:

1) Hartz will submit a letter of intent with a proposed schedule for submission of key elements discussed (including raw data for the NERL studies, a data development proposal, and a schedule for data development) by Tuesday 7/18/17
2) Hartz will submit to EPA the NERL data cited in its slides (with raw data) for EPA's review (NERL studies received post-meeting, awaiting raw data)
3) Hartz will submit a data development proposal and a schedule for data development (date not yet determined)
4) EPA will send contact information for Neil and Melissa, who are the alternate contacts while Khue is on vacation (completed post-meeting)

Exhibit W

TCVP: notes from teleconference with Hartz—8/7/17

EPA and Hartz discussed Hartz' 7/18/17 data development proposal and EPA's recent comments sent on the morning of 8/7/17. Hartz indicated that it would need more time to review EPA's comments, but had some initial thoughts. With respect to item 1 (Hartz' proposal that contact time/duration of young children measured by NERL be used in pet exposure calculations), Hartz acknowledged the limitations with respect to the Beamer et al 2008 and Au Yeung et al 2007 studies, but thought those limitations could be remedied with more information on the data used in the studies. EPA should consider these studies as part of a weight of evidence and an area of refinement.

With respect to item 2 (use of biomonitoring data from the Davis 2008 study), Hartz disagrees with EPA's current stance on this. PBPK modeling can be done with TCVP and the CFR doesn't exclude the use of biomonitoring data. Hartz wanted to follow up on this and figure out how to explore this option, possibly by generating a model of the kinetics. EPA said the data would need to go through the human studies review board (HSRB), which previously identified issues with recruiting for such studies, and EPA had poor reception of similar data in the past. EPA was not interested in exploring this option.

With respect to item 3 (mass balance issue with EPA's current assessment methodology for pet collars), Hartz thought there were additional aspects to consider and wanted to follow up further. Hartz thought reasonable assumptions could be made on residue amounts on the individual or in the environment. EPA reiterated its belief that the mass balance issue would be addressed with the additional data on the release rate of TCVP and the mechanical stress/torsion study that was being proposed.

With respect to item 4 (proposed data development), Hartz stated that it was not committing to conduct a study to evaluate the weight percentage of TCVP and other components from TCVP collars following torsion/mechanical stress. It had recently received the protocol from Bayer for this study and was concerned about the science. The study does not meet the needs of Hartz' pet collar product—torsion is an extreme condition that pet collars would not likely to be exposed to. Hartz stated it would need to talk to Bayer before committing to conduct this study.

In general, out of all the options being explored, Hartz was in favor of item 3 (addressing the mass balance issue) by attempting to determine a transfer coefficient for the TCVP collar. EPA thinks this option was associated with too much uncertainty and would involve a longer-term endeavor. This option would give info on how much TCVP is released from the collar, but won't give info on if the TCVP released is liquid or solid and the proportion of each, which was a key uncertainty in risk assessment.

EPA was interested in how much TCVP can come off a collar in a day's time. The mass balance issue would be addressed as a consequence of the torsion study, but it was not the key item to focus on. EPA suggests a shorter timeframe for a study (30 days) instead of a longer study. The key is what is being released and whether it was liquid or solid. If Hartz disagreed with Bayer's approach, it should come up with its own proposal for measuring how much solid will be released from the TCVP collar, and determine the composition of the solid.

Hartz asked EPA whether/how these data development discussions would influence the release of the PID currently slated for September 2017. EPA was willing to roll back the timeline for decision-making for TCVP, provided that Hartz move forward with a short-term study (30 days) to examine the release

rate of TCVP from pet collars and conduct the TCVP torsion study. EPA prioritized the following info: the rate of release of TCVP, the % solid released, and the composition of the solid.

EPA was not willing to wait a long time for data in order to move forward with decision-making. It was not willing to revisit existing SOPs. TCVP has had multiple risk assessments, multiple public comment periods, and EPA first identified the problem with the liquid vs. dust composition question a couple years ago in discussions with all TCVP technical registrants. The information submitted through info requests did not address this uncertainty. EPA also needed to respond to NRDC's petition.

EPA will wait for short-term data, but it needed firm agreement from Hartz. Hartz said it would review Bayer's protocol, consult with Bayer, think about the options discussed, and get back to EPA. Hartz would need at least a week. Another teleconference call was discussed, possibly around August 16th, before any protocol submission. Hartz will get back to EPA on the timing of its response by the end of 8/8/17.

Exhibit X

2018 Registration Review Schedule for Conventional Cases (as of 09/18/2017)

Draft Risk Assessments	Proposed Interim Decisions	Interim Decisions
Quarter 1		
• Niclosamide (Eco only) • TFM/Lampricide (Eco only) • Thiobencarb • Glyphosate • Acetamiprid • Fenhexamid • Pyrithiobac • Ametryn • Prometon • Diphenylamine • Cypermethrin • Methomyl • Thiodicarb • Pymetrozine • Butralin	• Linuron	• Bromuconazole • Mepiquat Chloride/Pentaborate • Aldicarb • Pronamide • Carfentrazone-ethyl • Ethephon • Hexazinone • Spinosad • Spinetoram
Quarter 2		

2018 Registration Review Schedule for Conventional Cases (as of 09/18/2017)

• Pyridaben • Terbacil • Diflubenzuron • Prohexadione calcium • Flucarbazone • Amitraz • Propazine (Human Health only) • Atrazine (Human Health only) • Simazine (Human Health only) • Flumethrin	• Asulam • EPTC • Bromacil • Prometryn • Propamocarb	• Nitrapyrin • Pendimethalin • Cloransulam • Clodinafop-propargyl • Noviflumuron • Cyclanilide • Flumiclorac • Metaflumizone • Dimethomorph • Methoxyfenozide • Azoxystrobin • Coppers • Boric Acid • Diquat Dibromide • Fomesafen • Metalaxyl/Mefenoxam
Quarter 3		

2018 Registration Review Schedule for Conventional Cases (as of 09/18/2017)

• MCPA • Trifluralin • Fluthiacet-methyl • Imazalil & Imazalil sulfate • Oxytetracycline • Streptomycin • Dimethyl Disulfide (DMDS) • Pyrimidinone (Hydramethylnon) • Captan • Paraquat dichloride • Chloropicrin • Fenpyroximate • Prodiamine • Dithiopyr • TPTH • Cyhalofop-butyl (Human Health only) • Acibenzolar	• Benfluralin • 2,4-D • Oryzalin • Chlorpropham • Dichlobenil • Dinotefuran • Imidacloprid • Thiamethoxam • Clothianidin • Fludioxinil • Fluopicolide • Abamectin • Emamectin • Buprofezin • Pyriproxyfen • Diflufenzopyr • Lufenuron • Indoxacarb • Trifloxystrobin • Oxamyl • Metribuzin	• Linuron • Cymoxanil • Kresoxim-methyl
Quarter 4		

2018 Registration Review Schedule for Conventional Cases (as of 09/18/2017)

- Fluroxypyr,1-methylheptylester
- Formetanate HCl
- Bromoxynil and esters
- Methyl isothiocyanate (MITC)
- Methyldithiocarbamate salts (metam sodium)
- Dazomet
- Starlicide
- 2,4-DP
- 2,4-DB
- Naphthalene
- Methanearsonic acid, salts (MSMA)

- Niclosamide
- TFM/Lamprecide
- Thiobencarb
- Glyphosate
- Fluridone
- Emamectin Benzoate
- Quinoxyfen
- Ametryn
- Carbaryl
- Prometon
- Pyrithiobac
- Pymetrozine
- Butralin
- Norflurazon
- Methiocarb
- PBO
- Diphenylamine
- d-Phenothrin
- Cyphenothrin
- Fenpropathrin
- Imiprothrin
- Prallethrin
- Cyhalothrins (gamma and lambda)
- Etofenprox
- Cypermethrin
- Cyfluthrins
- Permethrin
- Tefluthrin
- Esfenvalerate
- Tau-fluvalinate
- Tetramethrin
- Deltamethrin
- Momfluothrin
- Pyrethrins
- Bifenthrin
- Flumethrin

- Asulam
- EPTC
- Metribuzin
- Bromacil
- Prometryn
- Propamocarb

Exhibit Y

2018-2019 Registration Review Schedule for Conventional Cases (as of 09/19/2018)

Draft Risk Assessments	Proposed Interim Decisions	Interim Decisions
Quarter 4 FY2018		

2018-2019 Registration Review Schedule for Conventional Cases (as of 09/19/2018)

• Atrazine (Human Health only) • Propazine (Human Health only) • Simazine (Human Health only) • Bispyribac • Imazamox • Imazapic • Imazaquin • Imazethapyr • Florasulam • Flucarbazone • Penoxsulam • Captan • Chloropicrin • Fluroxypyr,1-methylheptylester • Formetanate HCl • Bromoxynil and esters • Methyldithiocarbamate salts (metam sodium) • Dazomet • MCPA • Starlicide • Paradichlorobenzene • Diphenylamine • TPTH • Cyhalofop-butyl (Human Health only) • Prodiamine • Imazalil & Imazalil sulfate • Amitraz • Sodium Cyanide • Sodium Fluoroacetate • M-cresol • Xylenol	• Abamectin • Buprofezin • Ametryn • Oryzalin • Pyrithiobac • Butralin • Methiocarb • Diphenylamine • Cyhalofop-butyl (Human Health only) • Prodiamine • Sodium Cyanide • Sodium Fluoroacetate • Thiobencarb • M-cresol • xylenol	• Acibenzolar-s-methyl • Asulam • EPTC • Fludioxonil • Propamocarb • Niclosamide • TFM/Lampricide • Coppers

Quarter 1 FY2019

2018-2019 Registration Review Schedule for Conventional Cases (as of 09/19/2018)

- 2,4-DP
- 2,4-DB
- Aliphatic solvents
- Clopyralid
- Dimethyl Disulfide (DMDS)
- Flumioxazin
- Methomyl
- Methyl Bromide
- Naphthalene
- Paraquat dichloride
- Phenmedipham
- Thiodicarb

- 2,4-D
- Diflubenzuron
- Glyphosate
- Linuron
- Lufenuron
- Prohexadion calcium
- Pymetrozine
- Tebuthiuron

- Azoxystrobin
- Chlorpropham
- Coumaphos
- Dichlobenil
- Diflufenzopyr
- Fenhexamid
- Fluopicolide
- Indoxacarb
- Prometryn
- Trifloxystrobin

Quarter 2 FY2019

- Fenbutatin Oxide
- Fenamidone
- Isoxaflutole
- MCPB
- Oxyfluorfen
- Oxytetracylcine
- Phostebupirim
- Propanil
- Propargite
- Pyraclostrobin
- Streptomycin
- Sulfuryl Fluoride
- Thiabendazole
- Zoxamide

- Acetamiprid
- Bispyribac-sodium
- Clothianidin
- Dinotefuran
- Dithiopyr
- Florasulam
- Flucarbazone
- Fluthiacet-methyl
- Imazamox
- Imazapic
- Imazaquin
- Imazethapyr
- Imidacloprid
- Oxytetracylcine
- Penoxsulam
- Pyridaben
- Pyrimidinone (hydramethylon)
- Streptomycin
- Thiamethoxam
- Trifluralin

- Abamectin
- Ametryn
- Benfluralin
- Buprofezin
- Butralin
- Clomazone
- Cyhalofop-butyl
- Diphenylamine
- Emmamectin benzoate
- Fluridone
- m-cresol
- Methiocarb
- Oryzalin
- Oxamyl
- Prodiamine
- Pyrithiobac
- Sodium cyanide
- Sodium fluoroacetate
- Spinosad
- Spinetoram
- Thiobencarb
- Xylenol

2018-2019 Registration Review Schedule for Conventional Cases (as of 09/19/2018)

Quarter 3 FY2019

- 1,3-D
- Carboxin
- Cyazofamid
- Cyproconazole
- Dikegulac sodium
- Etoxazole
- Etridiazole (Terrazole)
- Flonicamid
- Lime sulfur
- Mecoprop (MCPP)
- Mesotrione
- Myclobutanil
- Pinoxaden
- Propylene oxide
- Pyraflufen-ethyl
- Terbacil
- Thiophanate-methyl
- Uniconazole

- Amitraz
- Bifenthrin
- Bromacil
- Bromoxynil and esters
- Captan
- Chloropicrin
- Cyfluthrins
- Cyphenothrin
- Cypermethrins
- Deltmathrin
- Diclosulam
- DMDS
- Dazomet
- Esfenvalerate
- Fenpropathrin
- Flumethrin
- Fluroxypyr
- Gamma-cyhalothrin
- Imazalil
- Imiprothrin
- Lambda-cyhalothrin
- Methyldithiocarbamate salts (metam sodium)
- Metribuzin
- Momfluorothrin
- PBO
- p-Dichlorobenzene
- Permethrin
- Phenothrin
- Prometon
- Pyrethrins
- Tau-fluvalinate
- Tefluthrin
- Tetramethrin
- TPTH

- 2,4-D
- Diflubenzuron
- Diquat Dibromide
- Linuron
- Lufenuron
- Prohexadion-calcium
- Pymetrozine
- Pyridaben
- Tebuthiuron

Quarter 4 FY2019

2018-2019 Registration Review Schedule for Conventional Cases (as of 09/19/2018)

• Acequinocyl • Acetochlor • Boscalid • Chlorothalonil • Ethoxyquin • Famoxadone • Fenpyroximate • Fluazifop butyl • Iprodione • Metolachlor & s-Metolachlor • Sethoxydim • Spiromesifen • Triclopyr	• 2,4-DP • 2,4-DB • Aliphatic Solvents • Atrazine • Clopyralid • Flumioxazin • Formetanate • MCPA • Methomyl • Methyl Bromide • Napthalene • Norflurazon • Propargite • Propazine • Simazine • Terbacil • Thiodicarb	• Bispyribac-sodium • Clothianidin • Dithiopyr • Florasulam • Flucarbazone • Fluthiacet-methyl • Glyphosate • Imazamox • Imazapic • Imazaquin • ImazethapyrImidaclopri • Oxytetracylcine • Penoxsulam • Pyridaben • Pyrimidinone (hydramethylon) • Pyriproxyfen • Streptomycin • Trifluralin

2018-2019 Registration Review Schedule for Antimicrobial Cases (as of 09/25/2018)

Draft Risk Assessments	Proposed Interim Decisions	Interim Decisions
Quarter 4 FY2018		

Exhibit Z

2019-2020 Registration Review Schedule for Conventional Cases (as of 03/26/2019)

Draft Risk Assessments	Proposed Interim Decisions	Interim Decisions
Quarter 1 FY2019		
• 2,4-DB • Aliphatic solvents • Dimethyl Disulfide (DMDS) • Methomyl • Methyl Bromide • Naphthalene • Oxytetracycline • Phenmedipham • Streptomycin • Thiodicarb	• Buprofezin • Diflubenzuron • Lufenuron • Oxytetracycline • Prohexadione calcium • Pymetrozine • Streptomycin • Tebuthiuron • Thiobencarb	• Azoxystrobin • Benfluralin • Chlorpropham • Clomazone • Dichlobenil • Diflufenzopyr • Fenhexamid • Fluopicolide • Fluridone • Indoxacarb • Prometryn • Trifloxystrobin • Spinosad • Spinetoram
Quarter 2 FY2019		

2019-2020 Registration Review Schedule for Conventional Cases (as of 03/26/2019)

• 2,4-DP • Clopyralid • Flumioxazin • Thiabendazole • Zoxamide	• Aliphatic solvents • Bispyribac-sodium • Diclosulam • Florasulam • Flucarbazone • Glyphosate • Imazamox • Imazapic • Imazaquin • Imazethapyr • Penoxsulam • Pyrimidinone (hydramethylon) • Trifluralin	• Cyhalofop-butyl • Emamectin benzoate • m-cresol • Prodiamine • Xylenol

Quarter 3 FY2019

2019-2020 Registration Review Schedule for Conventional Cases (as of 03/26/2019)

• Carboxin • Cyazofamid • Cyproconazole • Dikegulac sodium • Etoxazole • Etridiazole (Terrazole) • Fenamidone • Fenbutatin Oxide • Flumetralin • Lime sulfur • MCPB • Mecoprop (MCPP) • Oxyfluorfen • Paraquat dichloride • Pinoxaden • Propanil • Pyraclostrobin • Pyraflufen-ethyl • Uniconazole	• Acetamiprid • Bromoxynil and esters • Clothianidin • Dinotefuran • Fluthiacet-methyl • Imazalil • Imidacloprid • Linuron • Pyridaben • Starlicide • Thiamethoxam	• Abamectin • Ametryn • Butralin • Coumaphos • Diquat Dibromide • Diphenylamine • Lufenuron • Methiocarb • Oryzalin • Prohexadione calcium • Pyrithiobac • Sodium cyanide • Sodium fluoroacetate • Tebuthiuron

Quarter 4 FY2019

2019-2020 Registration Review Schedule for Conventional Cases (as of 03/26/2019)

- Acequinocyl
- Acetochlor
- Boscalid
- Ethoxyquin
- Fenpyroximate
- Flonicamid
- Fluazifop butyl
- Iprodione
- Metolachlor & s-Metolachlor
- Myclobutanil
- Phostebupirim
- Propargite
- Sethoxydim
- Spiromesifen
- Spirodiclofen
- Terbacil
- Triallate
- Triclopyr

- 2,4-D
- 2,4-DB
- Atrazine
- Bifenthrin
- Captan
- Chloropicrin
- Clopyralid
- Cyfluthrins
- Cypermethrins
- Cyphenothrin
- Deltamethrin
- DMDS
- Dazomet
- Esfenvalerate
- Etofenprox
- Fenpropathrin
- Flumethrin
- Fluoxypyr
- Formetanate
- Gamma-cyhalothrin
- Imiprothrin
- Lambda-cyhalothrin
- MCPA
- Methomyl
- Methyl Bromide
- Methyldithiocarbamate salts (metam sodium)
- Momfluorothrin
- Napthalene
- P-Dichlorobenzene
- Phenmedipham
- Prallethrin
- PBO
- Phenothrin
- Propazine
- Pyrethrins
- Simazine
- Tau-fluvalinate
- Tefluthrin
- Tetramethrin
- Thiodicarb
- TPTH

- Aliphatic solvents
- Bispyribac-sodium
- Buprofezin
- Diclosulam
- Diflubenzuron
- Dithiopyr
- Florasulam
- Flucarbazone
- Glyphosate
- Imazamox
- Imazapic
- Imazaquin
- Imazethapyr
- Oxamyl
- Oxytetracycline
- Penoxsulam
- Prohexadione-calcium
- Pymetrozine
- Pyrimidinone (hydramethylon)
- Pyriproxyfen
- Streptomycin
- Thiobencarb
- Trifluralin

2019-2020 Registration Review Schedule for Conventional Cases (as of 03/26/2019)

Quarter 1 FY2020

• 1,3-D • Cycloate • Fipronil • Oxadiazon • Thiophanate-methyl • Topramezone (BAS 670H) • Triticonazole	• 2,4-DP • Etridiazole • Flumioxazin • Metribuzin • Pyraclostrobin • Thiabendazole • Zoxamide	• Acetamiprid • Bromoxynil and esters • Clothianidin • Dinotefuran • Fluthiacet-methyl • Imazalil • Imidacloprid • Linuron • Pyridaben • Starlicide • Thiamethoxam

2019 Registration Review Schedule for Antimicrobial Cases (as of 03/20/2019)

Draft Risk Assessments	Proposed Interim Decisions	Interim Decisions

Quarter 1 FY2019

CERTIFICATE OF SERVICE

I hereby certify that I have this date served a copy of the foregoing Appendix upon all parties by U.S. mail at the following addresses:

Matthew Z. Leopold, General Counsel
Environmental Protection Agency
1200 Pennsylvania Avenue NW
Mail Code: 2310A
Washington, DC 20460

Andrew Wheeler, Administrator
Environmental Protection Agency
1200 Pennsylvania Avenue NW
Mail Code: 1101A
Washington, DC 20460

William P. Barr, Attorney General
U.S. Department of Justice
950 Pennsylvania Avenue NW
Washington, DC 20530

Civil Process Clerk
U.S. Attorney's Office for the Northern District of California
450 Golden Gate Avenue, 11th Floor
San Francisco, CA 94102

Dated: May 29, 2019

/s/ *Jessie Baird*
Jessie Baird